IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

SEPRACOR INC., Plaintiff, v. DEY, L.P. and DEY, INC., Defendants.	C.A. No. 06-113-KAJ

PLAINTIFF SEPRACOR INC.'S ANSWERING BRIEF IN OPPOSITION TO DEFENDANTS DEY, L.P.'S AND DEY, INC.'S MOTION TO STRIKE ALLEGATIONS CONCERNING WILLFUL INFRINGEMENT

November 22, 2006

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Publications

This is the Answering Brief of Sepracor Inc. ("Sepracor") in opposition to the motion (D.I. 68), and memorandum (D.I. 69), of Dey, L.P. and Dey, Inc. (collectively "Dey") to strike certain paragraphs in Sepracor's complaint relating to Dey's willfulness and exceptional case.

I. FACTUAL BACKGROUND AND APPLICABLE LEGAL PRINCIPLES REGARDING HATCH-WAXMAN PARAGRAPH IV LITIGATIONS

This patent infringement suit involves Dey's copying of Sepracor's XOPENEX® (levalbuterol hydrochloride) inhalation solutions that are used to treat asthma, induce bronchodilation, and treat, prevent, or provide relief of bronchospasm. XOPENEX® (levalbuterol hydrochloride) inhalation solutions have been an enormous commercial success, with United States sales reaching almost $430 million per year in 2005. Sepracor's U.S. Patent Nos. 5,362,755; 5,547,994; 5,760,090; 5,844,002; and 6,083,993 (collectively, the "patents-in-suit") claim various methods of using XOPENEX® (levalbuterol hydrochloride) inhalation solutions.

Dey filed an Abbreviated New Drug Application ("ANDA") with the U.S. Food and Drug Administration ("FDA") – ANDA No. 77-800 – seeking approval to market generic copies of levalbuterol hydrochloride inhalation solutions, 0.31 mg/3 mL, 0.63 mg/3 mL, 1.25 mg/3 mL. *See* Complaint for Patent Infringement (D.I. 1) ¶ 16, at 4; Amended Answer and Counterclaims (D.I. 60) ¶ 16, at 3. Unlike Sepracor, the innovator company that had to file voluminous data with FDA to obtain approval of its XOPENEX® (levalbuterol hydrochloride) inhalation solutions as listed in the Orange

Book,[1] Dey, as the ANDA applicant, need only show that its proposed generic copy is "bioequivalent" to Sepracor's previously approved drug products and make one of four statements concerning Sepracor's previously approved drug products. 21 U.S.C. § 355(j)(2)(A)(iv). Dey filed its ANDA with a paragraph IV certification, that is, a statement that the patent(s) listed in the Orange Book for Sepracor's XOPENEX® (levalbuterol hydrochloride) inhalation solutions are "invalid or will not be infringed by the manufacture, use, or sale of the new drug" covered by the ANDA. 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

An ANDA applicant must "display care and regard for the strict standards of the Hatch-Waxman Act when challenging patent validity." *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1347 (Fed. Cir. 2000); *see also Takeda Chem. Indus., Ltd. v. Mylan Labs, Inc.*, Nos. 03-8253, 04-1966, 2006 WL 2686779, at *2 (S.D.N.Y. Sept. 20, 2006) (quoting *Yamanouchi*, 231 F.3d at 1347); *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.* No. 99-38, 2001 WL 1397304, at *16 (S.D. Ind. Oct. 12, 2001) (quoting *Yamanouchi*, 231 F.3d at 1347). These "challenges are only authorized 'in accordance with strict statutory requirements.'" *Takeda*, 2006 U.S. Dist. LEXIS 66990, at *4-5. In particular, the statute requires the challenger to state in the paragraph IV certification that "in the opinion of the applicant and to the best of his knowledge," each patent for which the applicant is seeking approval "is invalid or will not be infringed . . . ." 21 U.S.C. § 355(j)(2)(A)(vii)(IV). Therefore, the Hatch-Waxman Act holds such ANDA filers to a "'duty of due care.'" *Takeda*, 2006 U.S. Dist. LEXIS 66990, at *5.

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[1] *See* D.I. 1 ¶ 18, at 4 (identifying FDA's publication commonly known as the Orange Book).

An ANDA applicant must provide the patent owner a Notice Letter containing a "detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not infringe." 21 U.S.C. § 355(j)(2)(B)(iv)(II). In the present case, Dey sent Sepracor a letter dated January 9, 2006 providing notification that Dey filed its ANDA No. 77-800 with a paragraph IV certification. D.I. 1 ¶¶ 17-19, at 4. As part of this Notice Letter, Dey asserted more specific purported grounds on which it asserts that the patents-in-suit are invalid and/or not infringed. D.I. 1 ¶ 20, at 5. That Notice Letter prompted Sepracor to sue Dey, on February 22, 2006, to protect its proprietary rights. D.I. 1. Dey filed an answer to Sepracor's complaint on June 7, 2006 (D.I. 12) and an amended answer on October 23, 2006 (Attachment 1 to D.I. 56).

After considering this Court's decision in *Boehringer Ingelheim International GmBH v. Barr Laboratories, Inc*, No. 05-700, 2006 WL 1876918 (D. Del. July 6, 2006), counsel for Sepracor initiated a dialogue with counsel for Dey in order to be consistent with this Court's recent holding regarding willfulness in a paragraph IV patent litigation. In fact, counsel for Sepracor provided Dey's counsel with a copy of the Memorandum Order in the *Boehringer Ingelheim* case. *See* E-MAIL FROM DADIO TO LEFF ON AUG. 23, 2006 (Exhibit A). During these discussions with Dey's counsel, Sepracor acknowledged that the *Boehringer Ingelheim* case indicated that "an ANDA filing and accompanying paragraph IV certification[] cannot support a charge of willful infringement [for purposes of awarding attorney's fees pursuant to 35 U.S.C. § 271(e)(4)(A)-(C)]." *See, e.g.,* LETTER FROM DADIO TO LEFF DATED OCTOBER 26, 2006, at 2 (Exhibit B). However, 35 U.S.C. § 285 permits an award of attorney's fees to the prevailing party in exceptional cases, even when such cases are paragraph IV patent litigations. *See* 35 U.S.C. § 271(e)(4) (stating

"except that a court may award attorney fees under section 285"); *Glaxo Group Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1350 (Fed. Cir. 2004). Therefore, during these discussions with Dey's counsel, Sepracor's counsel continually emphasized that it would not withdraw its claim of exceptional case under section 285, *see* Exhibit B at 2, and "willfulness" is a basis, as well as other types of misconduct, for exceptional case, *see Yamanouchi Pharm.*, 231 F.3d at 1346-47. Sepracor's counsel even discussed with Dey's counsel the definitional uncertainties in the recent case law on this subject with respect to whether activity such as, for example, a baseless paragraph IV certification combined with other litigation conduct is considered "willfulness" or classified under another type of misconduct for purposes of an award of attorney fees.

Consistent with this Court's decision in the *Boehringer Ingelheim* case and consistent with the discussions between counsel for the parties, Sepracor prepared and sent to Dey's counsel a draft proposal for joint stipulation, "without prejudice[,] to stay discovery on facts related solely to Dey's willfulness for purposes of an exceptional case determination and an award of attorney's fees pursuant to 35 U.S.C. § 285[] . . . until such time as there is a prevailing party in the litigation."[2] *See* ATTACHMENT TO LETTER FROM DADIO TO LEFF DATED OCTOBER 26, 2006 (emphasis added) (Exhibit C).

Dey's counsel never came back with any revisions or specific comments on the draft proposal for joint stipulation. Instead, well after the filing of Dey's responsive pleadings, Dey has moved "[p]ursuant to Rule 12(f) of the Federal Rules of Civil Procedure" to strike certain paragraphs of Sepracor's complaint, in particular the paragraphs numbered 25 and 26, and the paragraph lettered D. DEY'S OPENING

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[2] Dey has accused Sepracor of "breaking" its agreement to withdraw willfulness without prejudice. Such allegations are simply not true. *See* Exhibit B.

MEMORANDUM IN SUPPORT OF ITS MOTION TO STRIKE PLAINTIFF'S CLAIM FOR WILLFUL INFRINGEMENT ("DEY'S OPENING BRIEF") at 1 & 5.

II. DEY'S MOTION TO STRIKE THE IDENTIFIED PARAGRAPHS IN SEPRACOR'S COMPLAINT SHOULD BE DENIED

A. Dey's Motion Improperly Attempts to Strike Sepracor's Claim of Exceptional Case

Motions to strike are generally viewed with disfavor because striking a portion of a pleading is a drastic remedy and because it is often sought simply as a harassing tactic. *See* 5C CHARLES ALAN WRIGHT & ARTHUR R. MILLER, FEDERAL PRACTICE AND PROCEDURE § 1380 (3d ed. 2004). Dey requests this Court to strike the following paragraphs from Sepracor's complaint (D.I. 1):

> 25. On information and belief, Dey, L.P.'s statement of the factual and legal basis for its opinion regarding the validity of the Sepracor Patents is devoid of an objective good faith basis in either the facts or the law.
>
> 26. On information and belief, in filing its ANDA No. 77-800 to obtain approval to engage in the commercial manufacture, use and/or sale of Dey's Levalbuterol Inhalation Solutions before the expiration of the Sepracor Patents, Dey, L.P.'s infringement of the Sepracor Patents is, has been and continues to be willful and deliberate.
>
> . . . .
>
> WHEREFORE, Sepracor prays for judgment as follows:
>
> . . . .
>
> (D) A judgment that Dey, L.P.'s and Dey. Inc.'s infringement of the Sepracor Patents was and is willful and that Sepracor is entitled to it reasonable attorneys' fees pursuant to 35 U.S.C. § 285.

All of these paragraphs, however, relate to Dey's "willfulness" as it pertains to exceptional case under section 285. Moreover, Sepracor is not claiming "willfulness" as it pertains to exceptional case based solely on Dey's filing of an ANDA application.

Rather, Sepracor's claim is based on Dey's wholly unjustified assertions in its Notice Letter, its failure to satisfy its obligation of due care, and its reliance on those arguments in this litigation. Sepracor's facts, as pled, are taken as admitted on a motion to strike. *See* 5C CHARLES ALAN WRIGHT & ARTHUR R. MILLER, FEDERAL PRACTICE AND PROCEDURE § 1380 (3d ed. 2004). Moreover, Rule 8(a) of the Federal Rules of Civil Procedure only requires "notice pleading." Sepracor's pleading of "willfulness" for purposes of exceptional case puts Dey on more than sufficient notice in accordance with Rule 8(a).

This Court specifically held, in the *Boehringer Ingelheim* case, that even if plaintiff's claims of willful infringement are stricken, this does not eliminate exceptional case. *Boehringer Ingelheim*, 2006 WL 1876918, at *2. However, should the Court strike numbered paragraphs 25 and 26, and lettered paragraph D, it would be eliminating Sepracor's claim of exceptional case. This result is not justified by the law, nor is it appropriate here.

B. Dey's Rule 12(f) Motion Should Be Denied Procedurally as Being Untimely

A motion to strike under Rule 12(f) must be made "before responding" to the challenged pleading. FED. R. CIV. P. 12(f). Here, Dey has responded to the challenged pleadings twice – once in its Answer and Counterclaims filed on June 7, 2006, and a second time in its Amended Answer and Counterclaims filed on October 23, 2006 – before it ever filed the subject motion under Rule 12(f). Thus, Dey's motion should be denied for failing to be timely filed.

C. Dey's Motion Should Have Been Unnecessary and Therefore Is a Waste of Judicial Resources

In its Opening Brief, Dey argues the policy behind Rule 12(f) motions stating that the functions of such motions to strike are "to avoid expenditure of time and money . . . ." D.I. 69, at 3. The irony of Dey's argument is that its motion to strike is the epitome of a wasteful expenditure of time and money. This is compounded by the fact that instead of providing productive comments or revisions to Sepracor's draft proposed stipulation, Dey filed this unnecessary motion to strike.

While this Court may, in its discretion, consider an untimely motion to strike, it should only do so in the interest of justice. *See Krauss v. Keibler-Thompson Corp.*, 72 F.R.D. 615, 617 (D. Del. 1976). Here, the interests of justice would not be so served.

III. CONCLUSION

For the foregoing reasons, the Court should deny Dey's motion to strike the paragraphs numbered 25 and 26, and the paragraph lettered D from Sepracor's complaint.

THE BAYARD FIRM

November 22, 2006

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CERTIFICATE OF SERVICE

The undersigned counsel certifies that, on November 22, 2006, he electronically filed the foregoing document with the Clerk of the Court using CM/ECF, which will send automatic notification of the filing to the following:

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The undersigned counsel further certifies that, on November 22, 2006, copies of the foregoing document were sent by email and hand to the above local counsel and by email and first class mail to the following non-registered participant:

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/s/ Richard D. Kirk (rk0922)
Richard D. Kirk

EXHIBIT A

Dadio, Susan

From: Dadio, Susan
Sent: Wednesday, August 23, 2006 5:21 PM
To: 'Leff, Elizabeth'
Subject: Sepracor v Dey
Attachments: Judge Jordan opinion 05-700.pdf

Elizabeth:

Further to our telephone discussion today, attached is the opinion that I referenced.

Sincerely,
Susan

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BOEHRINGER INGELHEIM INTERNATIONAL GMBH and BOEHRINGER INGELHEIM PHARMACEUTICAL, INC.,	)	
Plaintiffs and Counterclaim Defendants,	)	
v.	)	Civil Action No. 05-700-KAJ (Consolidated)
BARR LABORATORIES, INC., et al.	)	
Defendants and Counterclaim Plaintiffs.	)	

MEMORANDUM ORDER

Introduction

Before me is a Motion for Reconsideration (Docket Item ["D.I."] 39; the "Motion")[1] filed by defendant Mylan Pharmaceuticals Inc. ("Mylan") with respect to my previous ruling denying without prejudice Mylan's Motion to Strike Plaintiffs' Allegations Concerning Willful Infringement and to Bar All Discovery Relating Thereto (D.I. 8 in 05-854-KAJ; the "Motion to Strike"). For the reasons that follow, the Motion is treated as a renewal of the Motion to Strike, in which co-defendants Barr Laboratories, Inc. and Barr Pharmaceuticals Inc. (collectively "Barr") are deemed to join (*see* D.I. 55 at n. 1 ("Should the Court grant Mylan's motion, Barr will renew without delay its motion to

[1]By order dated January 31, 2006, Civil Actions 05-700-KAJ and 05-854-KAJ were consolidated. (D.I. 33 in 05-700-KAJ.) Unless otherwise noted, citations to docket entries are to the docket in Civil Action No. 05-700-KAJ.

strike Boeringer's willfulness allegations.")), and is hereby granted to the extent described herein.

Background

This is a patent infringement case in which the plaintiffs, Boehringer Ingelheim International GmbH and Boehringer Ingelheim Pharmaceutical Inc. (collectively "Boehringer"), assert that Mylan and Barr have infringed certain United States Patents owned by Boehringer. (*See* D.I. 1 at ¶¶ 18, 23.)[2] More specifically, Boehringer alleges that Barr has infringed Boehringer's U.S. Patents No. 4,886,812 (the "'812 patent") and No. 4,843,086 (the "'086 patent") by filing abbreviated new drug applications ("ANDAs") with the FDA, in an effort to market generic versions of drugs covered by those Boehringer patents. (*Id.* at ¶¶ 11-16, 18, 23.) Boehringer alleges essentially the same thing against Mylan with respect to the '812 patent. (D.I. 1 in 05-854-KAJ.) According to Boehringer, the defendants' infringement is willful (*id.* at ¶¶ 20, 25), and Boehringer therefore seeks, among other things, a declaration that this is an exceptional case warranting the imposition of Boehringer's attorneys' fees on the defendants. (*Id.* at *ad damnum* ¶¶ B. and E.) Both Mylan and Barr sought to strike the allegations of willfulness. (D.I. 9; D.I. 8 in 05-854-KAJ.) I denied those motions on January 27, 2006.

Standard of Review

"Motions for reconsideration are to correct manifest errors of law or fact or to present newly discovered evidence." *Pell v. E.I. DuPont De Nemours & Co., Inc.*, 231

[2]The allegations recited herein are effectively the same in the Amended Complaint filed against Barr. (*See* D.I. 7.)

F.R.D. 186, 188 (D.Del. 2005). The party seeking reconsideration must show "at least one of the following grounds: (1) an intervening change in the controlling law; (2) the availability of new evidence that was not available when the court granted the motion ...; or (3) the need to correct a clear error of law or fact or to prevent manifest injustice." *Max's Seafood Cafe v. Quinteros,* 176 F.3d 669, 677 (3d Cir.1999).

Mylan has shown none of the applicable foundations for the granting of a motion for reconsideration. However, when I denied Mylan's Motion to Strike in the first instance, I expressly stated that the denial was "without prejudice" (1/27/06 Tr. at 11; *see also* D.I. 32),[3] since I viewed the motions as "premature because I don't know what besides the filing of an ANDA might be in the mix here." (1/27/06 Tr. at 11.) The submissions of the parties have made it sufficiently clear to me that no other basis exists for the assertion of willfulness besides the defendants' filing of ANDAs and so I will accept the Motion as a renewed motion to strike on behalf of all of the defendants, which was expressly contemplated by my earlier ruling, rather than as a motion to reconsider the first denial.

Discussion

Since the decision by the United States Court of Appeals for the Federal Circuit in *Glaxo Group Ltd. v. Apotex, Inc.*, 376 F.3d 1339 (Fed. Cir. 2004), defendants in patent cases based on ANDA filings have regularly sought to dismiss charges of willfulness. They, like Mylan and Barr in this case, base their arguments on the *Glaxo* court's comment that "the mere filing of an ANDA cannot constitute grounds for a willful

[3]References to "1/27/06 Tr." are to the transcript of the January 27, 2006 teleconference in this case.

infringement determination." *Id.* at 1349. The district courts have split on the issue. *See Celgene Corp. v. Teva Pharms. USA, Inc.*, 412 F. Supp. 2d 439, 444-45 (D.N.J. 2006) (collecting cases).

The more recent and growing weight of authority however, seems to be that an ANDA filing and accompanying paragraph IV certification[4] cannot support a charge of willful infringement. *See, e.g., UCB Societe Anonyme v. Mylan Labs., Inc.*, No. 1:04-CV683-WSD, 2006 WL 486895, at *2 (N.D. Ga. Feb. 28, 2006) ("Applying *Glaxo* ..., [plaintiff's] allegations cannot support a claim of willful infringement."); *Celgene*, 412 F. Supp. 2d at 445 ("The *Glaxo* case makes clear that the Hatch-Waxman Act exists ... to permit the matter [of infringement] to be decided before the drug goes to market and an actual, rather than artificial, act of infringement occurs."); *Aventis Pharma Deutschland GMBH v. Lupin Ltd.*, 409 F.Supp.2d 722, 729 (E.D. Va. 2006) ("[T]he fact that the appellate court in *Glaxo* emphasizes that the purpose of the ANDA process is to create an 'artificial' act of infringement for jurisdictional purposes strongly supports this Court's conclusion that even a baseless ANDA filing may never constitute willful infringement."). That includes recent decisions from this court. *See Item Dev. AB v. Sicor Inc.*, No. Civ. 05-336-SLR, 2006 WL 891032, at *2 (D. Del. Mar. 31, 2006) (because the filing of an ANDA and paragraph IV certification by defendant "cannot support a claim of willful infringement, plaintiffs' complaint fails to state a claim on that basis."); *Allergan, Inc. v. Alcon, Inc.*, No. 04-968, 2005 WL 3971927, at *2 (D. Del. July 25, 2005) ("As the

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[4]A paragraph IV certification is a submission made with an ANDA filing, by which a generic drug manufacturer asserts that a patent on a previously FDA-approved drug is invalid or will not be infringed by the proposed generic drug. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

Federal Circuit explained in *Glaxo,* a finding that a ANDA/paper NDA case is 'exceptional' can be based on meritless filings combined with litigation misconduct, but a finding of willful infringement cannot.").[5]

In light of that authority, which is persuasive, the plaintiffs' willfulness claims cannot stand and the motion to strike those claims will be granted. This does not, however, eliminate the question of whether there may, at some point, be occasion to find that this is an exceptional case. *See Item Dev.,* 2006 WL 891032, at *2 ("As the Federal Circuit explained in *Glaxo,* a finding that a ANDA/paper NDA case is 'exceptional' can be based on meritless filings combined with litigation misconduct, although a finding of willful infringement cannot.") (citing *Glaxo,* 376 F.3d at 1350-51); *Allergan*, 2005 WL 3971927, at *2 ("[T]he court will not foreclose Allergan from, at the appropriate time, seeking to prove additional facts that would support its claim of an exceptional case for which the court should award attorney's fees."). That decision must wait, since the issue may be determined, at least in part, on the conduct of the parties during the litigation of the case. Because it may also be unnecessary to ever decide the issue, the costs associated with discovery on it should be postponed.

Conclusion

Accordingly, based on the foregoing reasons and authorities, it is hereby ORDERED that the Motion (D.I. 39), treated as a renewed Motion to Strike in which Barr joins, is hereby GRANTED to the extent described herein; it is further ORDERED

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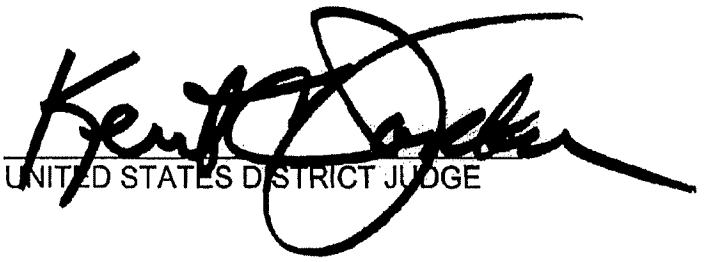
[5]I have had occasion to issue an oral ruling to that effect as well. *In re '318 Patent Infringement Lit.*, C.A. No. 05-356-KAJ (D. Del. Mar. 3, 2006) (hearing transcript at 4-7).

that all discovery associated with whether this is an "exceptional case" within the meaning of 35 U.S.C. § 285 is stayed.



UNITED STATES DISTRICT JUDGE

July 6, 2006
Wilmington, Delaware

EXHIBIT B

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October 26, 2006

VIA ELECTRONIC MAIL

Elizabeth A. Leff, Esq.
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1667 K Street, N.W.
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Re: *Sepracor Inc. v. Dey, L.P. and Dey, Inc.*
Civil Action No. 06-113 KAJ

Dear Elizabeth:

This is in response to your letter dated October 25, 2006 regarding Sepracor's allegations of willful infringement and our discussions regarding such allegations in light of Judge Jordan's decision in *Boehringer Ingelheim International GmbH v. Barr Laboratories, Inc.*, No. 05-700-KAJ (D. Del. July 6, 2006).

Let it be clear that Sepracor is not "breaking [any] agreement."

As you may recall, our discussions regarding an agreement on the willful infringement issue also included Dey's request to extend the due date for amendment of pleadings. Specifically, during our telephone discussion on September 1, 2006, you indicated that Dey wanted Sepracor to agree to a forty-five to sixty day extension of the due date for amending the pleadings in exchange for any agreement concerning Dey's willful infringement.

To follow up on Dey's request, we contacted you on September 6, 2006 via telephone so as to inquire about Dey's "need" for an extension of that length. You responded by stating that Dey "needed to serve requests for admissions" on Sepracor in order to obtain a "good faith basis" to add a claim of inequitable conduct. You went on to explain that it would take time to prepare and serve the requests for admissions, Sepracor would have thirty days to respond, and then Dey would have to review and consider such responses before Dey's pleadings could be amended. However, you stated that if Sepracor would agree to respond to such requests for admissions in less than thirty days, the time period could be shortened. We stated that it was difficult to know whether we could respond in less than thirty days without understanding what the requests for admissions looked like. You were unable to provide us with any insight at that time because you

stated that "you had not yet prepared them." Moreover, we explicitly asked at that time whether you were going to take any depositions during this time period. Your response was "no."

Based on your representations, we stipulated to a forty-six day extension of the due date (*i.e.*, until October 23, 2006) for amendment of the pleadings. We received notice in the afternoon on September 7th that the stipulation was filed with the Court by your local counsel. Then, later that same evening and just hours after the stipulation was filed, we received Dey's request for admissions **and** three notices of deposition and subpoena from Dey.

In light Dey's course of conduct in this prior situation, we do not think Dey is any position to accuse Sepracor of going against its word.

Now, with respect to the issue of Dey's willful infringement, you are absolutely correct that the basis for our conversations was Judge Jordan's decision in the *Boehringer Ingelheim* case. In fact, you may recall that we sent you a copy of that decision by e-mail. *See* ELECTRONIC MAIL FROM DADIO TO LEFF ON AUG. 23, 2006. The *Boehringer Ingelheim* case seems to indicate that "an ANDA filing and accompanying paragraph IV certification[] cannot support a charge of willful infringement [for purposes of awarding attorney's fees pursuant to 35 U.S.C. § 271(e)(4)(A)-(C)]." *Boehringer Ingelheim*, No. 05-700, slip op. at 4 (July 6, 2006). The exception, however, is that 35 U.S.C. § 285 permits an award of attorney's fees to the prevailing party in exceptional cases, *see* 35 U.S.C. § 271(e)(4) (stating "except that a court may award attorney fees under section 285), and willfulness is a basis for exceptional case. Accordingly, in all of our conversations with you in this regard, we always emphasized that Sepracor would not withdraw willfulness as it pertained to exceptional case.

Further, you may recall that during our discussions regarding postponing discovery on willfulness as it pertains to exceptional case you informed us that it was your preference to "bifurcate" these types of issues. Moreover, we know that, in other paragraph IV cases, your firm as counsel for the generic company has moved to bifurcate discovery on willfulness and "postpone . . . identification of and discovery concerning any advice of counsel defense . . . . *Takeda Chem. Indus. Ltd. v. Alphapharm Pty. Ltd*, No. 04-1966, slip op. at 9 (S.D.N.Y. Sept. 26, 2006).

Consistent with our discussions regarding Judge Jordan's decision in the *Boehringer Ingelheim* case, we stated in our letter of October 20, 2006 that we were working on a draft proposal for joint stipulation, without prejudice, to stay discovery for exceptional case until such time as there is a prevailing party. *See Boehringer Ingelheim*, slip op. at 5 ("This does not, however, eliminate the question of whether there may, at some point, be occasion to find that this is an exceptional case. . . . Because it may also be unnecessary to ever decide the issue, the costs associated with discovery on it should be postponed."). Accordingly, enclosed herewith for your review and consideration is a draft proposal for a joint stipulation.

If you have any questions or comments regarding the draft proposal, please do not hesitate to contact us.

Sincerely,

BUCHANAN INGERSOLL & ROONEY PC

Susan M. Dadio

SMD/jlr
Enclosure

EXHIBIT C

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

SEPRACOR INC., Plaintiff, v. DEY, L.P. and DEY, INC., Defendants.	**C.A. No. 06-113-KAJ**

[PROPOSED] STIPULATION TO STAY DISCOVERY ON WILLFULNESS

Plaintiff Sepracor Inc. ("Sepracor") and Defendants Dey, L.P. and Dey, Inc. (collectively "Dey"), by their undersigned counsel and subject to the Court's approval, hereby stipulate without prejudice to stay discovery on facts related solely to Dey's willfulness for purposes of an exceptional case determination and an award of attorney's fees pursuant to 35 U.S.C. § 285. The stay shall extend until such time as there is a prevailing party in the litigation.

October __, 2006

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SO ORDERED:

Dated: _____

_____
Hon. Kent A. Jordan
United States District Court for the
District of Delaware

UNREPORTED CASES

Boehringer Ingelheim Int'l GmBH v. Barr Labs., Inc,
No. 05-700, 2006 WL 1876918 (D. Del. July 6, 2006)

Briefs and Other Related Documents
Boehringer Ingelheim Intern. GmbH v. Barr Laboratories, Inc.D.Del.,2006.Only the Westlaw citation is currently available.

United States District Court,D. Delaware.
BOEHRINGER INGELHEIM INTERNATIONAL GMBH and **Boehringer Ingelheim** Pharmaceutical, Inc., Plaintiffs and Counterclaim Defendants,
v.
BARR LABORATORIES, INC., et al. Defendants and Counterclaim Plaintiffs.
No. Civ.A. 05-700-KAJ.

July 6, 2006.

Jack B. Blumenfeld, Maryellen Noreika, Morris, Nichols, Arsht & Tunnell, Wilmington, DE, Kenneth G. Schuler, Sandy Choi, Steven C. Cherny, Amanda J. Hollis, Carisa S. Yee, Joel S. Neckers, Pro Hac Vice, for Plaintiffs and Counterclaim Defendants.
Adam Wyatt Poff, Young, Conaway, Stargatt & Taylor, Mary Matterer, Morris, James, Hitchens & Williams, Wilmington, DE, for Defendants and Counterclaim Plaintiffs.

MEMORANDUM ORDER

JORDAN, J.

Introduction

***1** Before me is a Motion for Reconsideration (Docket Item ["D.I."] 39; the "Motion") [FN1] filed by defendant Mylan Pharmaceuticals Inc. ("Mylan") with respect to my previous ruling denying without prejudice Mylan's Motion to Strike Plaintiffs' Allegations Concerning Willful Infringement and to Bar All Discovery Relating Thereto (D.I. 8 in 05-854-KAJ; the "Motion to Strike"). For the reasons that follow, the Motion is treated as a renewal of the Motion to Strike, in which co-defendants Barr Laboratories, Inc. and Barr Pharmaceuticals Inc. (collectively "Barr") are deemed to join (*see* D.I. 55 at n. 1 ("Should the Court grant Mylan's motion, Barr will renew without delay its motion to strike Boeringer's willfulness allegations.")), and is hereby granted to the extent described herein.

FN1. By order dated January 31, 2006, Civil Actions 05-700-KAJ and 05-854-KAJ were consolidated. (D.I. 33 in 05-700-KAJ.) Unless otherwise noted, citations to docket entries are to the docket in Civil Action No. 05-700-KAJ.

Background

This is a patent infringement case in which the plaintiffs, Boehringer Ingelheim International GmbH and Boehringer Ingelheim Pharmaceutical Inc. (collectively "Boehringer"), assert that Mylan and Barr have infringed certain United States Patents owned by Boehringer. (*See* D.I. 1 at ¶ ¶ 18, 23.) [FN2] More specifically, Boehringer alleges that Barr has infringed Boehringer's U.S. Patents No. 4,886,812 (the " '812 patent") and No. 4,843,086 (the " '086 patent") by filing abbreviated new drug applications ("ANDAs") with the FDA, in an effort to market generic versions of drugs covered by those Boehringer patents. (*Id.* at ¶ ¶ 11-16, 18, 23.) Boehringer alleges essentially the same thing against Mylan with respect to the '812 patent. (D.I. 1 in 05-854-KAJ.) According to Boehringer, the defendants' infringement is willful (*id.* at ¶ ¶ 20, 25), and Boehringer therefore seeks, among other things, a declaration that this is an exceptional case warranting the imposition of Boehringer's attorneys' fees on the defendants. (*Id.* at *ad damnum* ¶ ¶ B. and E.) Both Mylan and Barr sought to strike the allegations of willfulness. (D.I. 9; D.I. 8 in 05-854-KAJ.) I denied those motions on January 27, 2006.

FN2. The allegations recited herein are effectively the same in the Amended Complaint filed against Barr. (*See* D.I. 7.)

Standard of Review

"Motions for reconsideration are to correct manifest errors of law or fact or to present newly discovered evidence." *Pell v. E.I. DuPont De Nemours & Co., Inc.*, 231 F.R.D. 186, 188 (D.Del.2005). The party seeking reconsideration must show "at least one of the following grounds: (1) an intervening change in the controlling law; (2) the availability of new evidence that was not available when the court granted the motion ...; or (3) the need to correct a clear error of law or fact or to prevent manifest injustice." *Max's Seafood Cafe v. Quinteros*, 176 F.3d

669, 677 (3d Cir.1999).

Mylan has shown none of the applicable foundations for the granting of a motion for reconsideration. However, when I denied Mylan's Motion to Strike in the first instance, I expressly stated that the denial was "without prejudice" (1/27/06 Tr. at 11; *see also* D.I. 32),[FN3] since I viewed the motions as "premature because I don't know what besides the filing of an ANDA might be in the mix here." (1/27/06 Tr. at 11.) The submissions of the parties have made it sufficiently clear to me that no other basis exists for the assertion of willfulness besides the defendants' filing of ANDAs and so I will accept the Motion as a renewed motion to strike on behalf of all of the defendants, which was expressly contemplated by my earlier ruling, rather than as a motion to reconsider the first denial.

FN3. References to "1/27/06 Tr." are to the transcript of the January 27, 2006 teleconference in this case.

Discussion

***2** Since the decision by the United States Court of Appeals for the Federal Circuit in *Glaxo Group Ltd. v. Apotex, Inc.*, 376 F.3d 1339 (Fed.Cir.2004), defendants in patent cases based on ANDA filings have regularly sought to dismiss charges of willfulness. They, like Mylan and Barr in this case, base their arguments on the *Glaxo* court's comment that "the mere filing of an ANDA cannot constitute grounds for a willful infringement determination." *Id.* at 1349. The district courts have split on the issue. *See Celgene Corp. v. Teva Pharms. USA, Inc.*, 412 F.Supp.2d 439, 444-45 (D.N.J.2006) (collecting cases).

The more recent and growing weight of authority however, seems to be that an ANDA filing and accompanying paragraph IV certification [FN4] cannot support a charge of willful infringement. *See, e.g., UCB Societe Anonyme v. Mylan Labs., Inc.*, No. 1:04-CV683-WSD, 2006 WL 486895, at *2 (N.D.Ga. Feb.28, 2006) ("Applying *Glaxo* ..., [plaintiff's] allegations cannot support a claim of willful infringement."); *Celgene*, 412 F.Supp.2d at 445 ("The *Glaxo* case makes clear that the Hatch-Waxman Act exists ... to permit the matter [of infringement] to be decided before the drug goes to market and an actual, rather than artificial, act of infringement occurs."); *Aventis Pharma Deutschland GMBH v. Lupin Ltd.*, 409 F.Supp.2d 722, 729 (E.D.Va.2006) ("[T]he fact that the appellate court in *Glaxo* emphasizes that the purpose of the ANDA process is to create an 'artificial' act of infringement for jurisdictional purposes strongly supports this Court's conclusion that even a baseless ANDA filing may never constitute willful infringement."). That includes recent decisions from this court. *See Item Dev. AB v. Sicor Inc.*, No. Civ. 05-336-SLR, 2006 WL 891032, at *2 (D.Del. Mar.31, 2006) (because the filing of an ANDA and paragraph IV certification by defendant "cannot support a claim of willful infringement, plaintiffs' complaint fails to state a claim on that basis."); *Allergan, Inc. v. Alcon, Inc.*, No. 04-968, 2005 WL 3971927, at *2 (D.Del. July 25, 2005) ("As the Federal Circuit explained in *Glaxo*, a finding that a ANDA/paper NDA case is 'exceptional' can be based on meritless filings combined with litigation misconduct, but a finding of willful infringement cannot.").[FN5]

FN4. A paragraph IV certification is a submission made with an ANDA filing, by which a generic drug manufacturer asserts that a patent on a previously FDA-approved drug is invalid or will not be infringed by the proposed generic drug. *See* 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

FN5. I have had occasion to issue an oral ruling to that effect as well. *In re '318 Patent Infringement Lit.*, C.A. No. 05-356-KAJ (D.Del. Mar. 3, 2006) (hearing transcript at 4-7).

In light of that authority, which is persuasive, the plaintiffs' willfulness claims cannot stand and the motion to strike those claims will be granted. This does not, however, eliminate the question of whether there may, at some point, be occasion to find that this is an exceptional case. *See Item Dev.*, 2006 WL 891032, at *2 ("As the Federal Circuit explained in *Glaxo*, a finding that a ANDA/paper NDA case is 'exceptional' can be based on meritless filings combined with litigation misconduct, although a finding of willful infringement cannot.") (citing *Glaxo*, 376 F.3d at 1350-51); *Allergan*, 2005 WL 3971927, at *2 ("[T]he court will not foreclose Allergan from, at the appropriate time, seeking to prove additional facts that would support its claim of an exceptional case for which the court should award attorney's fees."). That decision must wait, since the issue may be determined, at least in part, on the conduct of the parties during the litigation of the case. Because it may also be unnecessary to ever

decide the issue, the costs associated with discovery on it should be postponed.

Conclusion

***3** Accordingly, based on the foregoing reasons and authorities, it is hereby ORDERED that the Motion (D.I.39), treated as a renewed Motion to Strike in which Barr joins, is hereby GRANTED to the extent described herein; it is further ORDERED that all discovery associated with whether this is an "exceptional case" within the meaning of 35 U.S.C. § 285 is stayed.

D.Del.,2006.
Boehringer Ingelheim Intern. GmbH v. Barr Laboratories, Inc.
Slip Copy, 2006 WL 1876918 (D.Del.)

Briefs and Other Related Documents (Back to top)

- 2005 WL 3242195 (Trial Pleading) Amended Complaint (Oct. 14, 2005) Original Image of this Document (PDF)
- 1:05cv00700 (Docket) (Sep. 26, 2005)

END OF DOCUMENT

UNREPORTED CASES

Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.
No. 99-38, 2001 WL 1397304 (S.D. Ind. Oct. 12, 2001)

Westlaw.
Not Reported in F.Supp.2d
Not Reported in F.Supp.2d, 2001 WL 1397304 (S.D.Ind.)
(Cite as: Not Reported in F.Supp.2d)

Briefs and Other Related Documents
Eli Lilly & Co. v. Zenith Goldline Pharmaceuticals, Inc.S.D.Ind.,2001.Only the Westlaw citation is currently available.

United States District Court,S.D. Indiana,Indianapolis Division.

ELI LILLY AND COMPANY and Reliant Pharmaceuticals, LLC, Plaintiffs,
v.
ZENITH GOLDLINE PHARMACEUTICALS, INC., Defendant.

No. IP 99-38-C H/K.

Oct. 29, 2001.

Allen R Baum, Durham, NC, Jan M Carroll, Barnes & Thornburg, Indianapolis, IN, Ronald L Grudziecki, R Danny Huntington, Burns Doane Swecker & Mathis, Alexandria, VA, David A Nelson, Latham & Watkins, Chicago, IL, for Plaintiffs.
Stephen E Arthur, Harrison & Moberly, Indianapolis, IN, William L Mentlik, Lerner David Littenberg Krumholz & Mentlik, Westfield, NJ, for Defendant.

FINDINGS OF FACT AND CONCLUSIONS OF LAW

DAVID F. HAMILTON, District Judge.

*1 In this action for patent infringement, plaintiffs Eli Lilly and Company and Reliant Pharmaceuticals, LLC have sued defendant Zenith Goldline Pharmaceuticals, Inc. for infringing U.S. Patent No. 4,375,547. The 547 patent claims a chemical compound called nizatidine, which is the active agent in plaintiffs' anti-secretory anti-ulcer drug, AXID® . Infringement is conceded. The two contested issues are (a) whether the 547 patent is invalid for obviousness, and if not, (b) whether Zenith has willfully infringed the 547 patent so as to make this an "exceptional case" in which attorneys' fees should be awarded to plaintiffs under 35 U.S.C. § 285. On both issues, the case is strikingly similar to *Yamanouchi Pharmaceutical Co. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339 (Fed.Cir.2000), in which the Federal Circuit affirmed findings of validity and willfulness regarding one of the three other patented drugs of the same class, called "H2 receptor antagonists."

The act of infringement was Zenith's filing of an amended Abbreviated New Drug Application (ANDA) with the Food and Drug Administration seeking permission to manufacture and sell nizatidine as a generic drug before the 547 patent expires. Zenith filed its amended ANDA under the Drug Price Competition and Patent Term Restoration Act of 1984, which is better known as the Hatch-Waxman Act. Relevant portions are codified in 21 U.S.C. § 355(j) and 35 U.S .C. § 271(d)-(e). In the amended ANDA, Zenith included what is called a "Paragraph IV" certification asserting that the 547 patent is invalid as obvious from the prior art. See 21 U.S.C. § 355(j)(2)(A)(vii)(IV). Pursuant to the Hatch-Waxman Act, Zenith also notified Lilly of its filing. Lilly promptly responded by filing a timely suit for infringement. See 21 U.S.C. § 355(j)(5)(B)(iii).

Federal question jurisdiction exists under 28 U.S.C. § § 1331 and 1338(a). The case was tried to the court September 10-13, 2001. The court now states its findings of fact and conclusions of law. The substance of a statement shall govern whether it is treated as a finding of fact or conclusion of law.

As explained in detail below, the court finds that the 547 patent is valid. Zenith's obviousness argument is based on pure hindsight and ignores the critical properties of nizatidine, which Zenith's own expert witness conceded could not be predicted from the compound's structure. There is also considerable objective evidence that nizatidine is not obvious, including commercial success, unexpected results, and the failure of others in the field.

The court also finds that Zenith's infringement was willful, making this an exceptional case in which Lilly should recover its attorneys' fees. Before its act of infringement, Zenith obtained from outside patent counsel an oral opinion of invalidity, but Zenith could not reasonably rely upon it. A written opinion provided five weeks after the act of infringement contained key errors and omissions, and the circumstances in which both the oral and written opinions were provided show that Zenith did not reasonably rely on advice of counsel.

I. *The 547 Patent and H2 Receptor Antagonists*

*2 The 547 patent for nizatidine was issued to Dr. Richard Pioch on March 1, 1983. Dr. Pioch worked

for Lilly and had previously assigned his rights to Lilly. The date of invention for the subject matter of claim 1 of the 547 patent is November 27, 1979. The 547 patent will expire on April 12, 2002.[FN1]

> FN1. After this lawsuit was filed, Lilly assigned its rights in the 547 Patent to Reliant Pharmaceuticals, LLC, which has joined as a plaintiff. Under its agreement with Reliant, Lilly retains the right to maintain the present suit. This entry treats Lilly and Reliant jointly under the name Lilly.

The 547 patent has only one claim, for nizatidine. The chemical name for nizatidine is N-methyl-N'-2-([2-(dimethylaminomethyl)-4-thiazolyl] methylthio)ethyl 2-nitro-1, 1-ethenediamine. (The structure is shown below at page 19.)

Nizatidine is an H2 receptor antagonist useful for treating peptic ulcers. The enzyme histamine is known to cause parietal cells in the gastric glands in the lining of the stomach to secrete gastric acid. The biological effect of gastric acid secretion results from interaction between histamine and structures in the parietal cells known as "H2 receptors." Although the sequence of proteins in H2 receptors is now known, the shape of the physical structure of the H2 receptors (resulting from the folding of the chain of proteins) still is not known, nor do scientists understand just how histamine causes the effect of gastric acid secretion.

Excessive gastric acid secretion can cause illnesses ranging from mild discomfort to extremely serious conditions. In the late 1960s, scientists at several major pharmaceutical companies were trying to develop compounds to treat these conditions by suppressing the gastric acid secretion that would otherwise be caused by histamine. Such compounds are called "H2 receptor antagonists" because they suppress the biological action of the H2 receptors.

The first successful H2 receptor antagonist was cimetidine, developed by SmithKline French laboratories in Great Britain. In 1988, one recipient of the Nobel Prize for Physiology or Medicine was Sir James W. Black, who led the effort that resulted in cimetidine.[FN2]

> FN2. The Nobel Prize was awarded for Black's work in developing receptor antagonists and the broadly applicable principles useful in developing drugs for a wide variety of conditions. The official announcement of the Nobel Prize specifically described the development of cimetidine:
> Starting from the structure of the histamine molecule Black developed a series of substances which effectively blocked the H2-receptor mediated effects, in particular the secretion of gastric acid. In 1972 Black and coworkers for the first time defined the H2 receptors by using agonists and antagonists. One of the first synthesized substances, metiamide, was found to heal peptic ulcer but it produced agranulocytosis on rare occasions. Subsequently (1975) Black succeeded in developing another substance, cimetidine, which was found to have a marked effect in the treatment of peptic ulcer but without this side-effect. Blocking of the H2-receptors introduced a new principle in the treatment of peptic ulcer, and a series of new drugs with the same mechanism or action has later been developed. As a consequence the need for surgical treatment of peptic ulcer has decreased significantly.
> See
> www.nobel.se/medicine/laureates/1988/press.html.

Cimetidine was approved by the FDA in 1977. It remains a commercial product today with the brand name TAGAMET® . Generic versions have been available since 1994, when the patent on cimetidine expired. Cimetidine turned out to cause some negative side effects, including metabolic blockage through the interference with particular liver enzymes that caused the buildup of certain drugs to toxic levels, and impotence and breast swelling in men when administered in high doses. Also, cimetidine had to be taken four times a day.

These disadvantages spurred a massive effort by virtually all major drug companies to find better second-generation H2 receptor antagonists. As of 1979, when Dr. Pioch invented nizatidine, cimetidine was still the only H2 receptor antagonist approved by the FDA for treating peptic ulcer disease in humans and was still the only H2 receptor antagonist commercially available in the United States.

Since 1979, the FDA has approved only three more H2 receptor antagonists for consumer use in the

United States: ranitidine, famotidine, and nizatidine. In 1983, the FDA approved ranitidine, which is also known as ZANTAC® . In 1986, the FDA approved famotidine, which is also known as PEPCID® . The FDA approved Lilly's nizatidine in 1988. Cimetidine, ranitidine, famotidine, and nizatidine were originally available only by prescription, but all four have since been approved for over-the-counter sale, although at lower doses. Generic versions of cimetidine, ranitidine, and famotidine were approved by the FDA in 1994, 1997, and 2001 respectively. Regardless of the outcome of this lawsuit, generic versions of nizatidine should be available beginning April 12, 2002, when the 547 patent will expire.

II. *Zenith's Act of Infringement*

***3** Defendant Zenith Goldline Pharmaceuticals, Inc., which is now known as IVAX Pharmaceuticals ("Zenith" in this entry), is a wholly-owned subsidiary of IVAX Corporation. Zenith produces and markets generic drugs.

On September 15, 1998, Zenith filed an Abbreviated New Drug Applications (ANDA) 75-461 with the Food and Drug Administration (FDA) seeking approval to market generic nizatidine. That original ANDA 75-461 contained what is called a "Paragraph III" certification. Zenith's Paragraph III certification stated that Zenith would not market nizatidine until the expiration of the 547 Patent. See 21 U.S.C. § 355(j)(2)(A)(vii)(III).

Three weeks later, on October 6, 1998, Zenith amended ANDA 75-461 to include a "Paragraph IV" certification, which asserted that the 547 patent is invalid. Zenith's Paragraph IV certification stated:
In accordance with section 505(j)(2)(A)(vii)(IV) of the Federal Food, Drug, and Cosmetic Act, and 21 CFR 314.94(a)(12)(k)(A)(4), Zenith Goldline certifies that the following patents are invalid, unenforceable, or will not be infringed by the manufacture, use or sale of Zenith Goldline's Nizatidine Capsules USP, 300 mg, for which this application is submitted.
• US Patent No. 4,375,547-Expiry Date: April 12, 2002
We will comply with the notification requirements defined in Section 505(j)(2)(B)(i), Paragraphs I and II of the Federal Food, Drug and Cosmetic Act, (Codified at 21 CFR 314.95(a)), and the content of our notice will conform to the requirements defined in 505(j)(2)(B)(ii), (Codified at 21 CFR 314.95(c)).

On November 19, 1998, Zenith sent Lilly a Patent Certification Notice Letter, which is required when a Paragraph IV certification is filed. Ex. 1070. The notice letter informed Lilly of Zenith's Paragraph IV certification and asserted that the sole claim of the 547 Patent is obvious over certain prior art references:With respect to the 547 patent, certification has been made to the FDA as called for by the Act, § 505(j)(2)(A)(vii)(IV), that claim 1 thereof is invalid as being obvious in view of, *inter alia, Durant* et al., U.S. Patent 4,046,907; *Price* et al., U.S. Patent 4,128,658; *Crenshaw* et al., U.S. Patent 4,375,248; Tobias O. Yellin et al. *ICI 125,211: A New Gastric Antisecretory Agent Acting on Histamine H2-Receptor,* 25 LIFE SCIENCES 2001 (1979); and J. Bradshaw et al., *Ranitidine (AH-19065); a new potent, selected histamine H2-Receptor antagonist,* PROCEEDINGS of B.P.S. 464P (1979). The composition of matter, nizatidine, is highly structurally similar to compounds disclosed in *Durant* et al., *Crenshaw* et al. and to ranitidine, and any differences therebetween are suggested by the prior art. In addition, the properties resulting from both ranitidine and nizatidine are highly analogous.

Within 45 days after receiving the notice letter, Lilly filed this suit against Zenith alleging infringement of the 547 patent under 35 U.S.C. § 271(e)(2)(A), and willful infringement under 35 U.S.C. § 285.

***4** Zenith has admitted that its act of amending ANDA 75-461 for nizatidine to add the Paragraph IV certification was an act of infringement of the 547 Patent under 35 U.S.C. § 271(e). See *Eli Lilly & Co. v. Medtronic, Inc.,* 496 U.S. 661, 676 (1990) (§ 271(e) defined new and "somewhat artificial" act of infringement for ANDA process).

III. *The Validity of the 547 Patent*

A. *The Law of Obviousness for Chemical Compounds*

The only issue on the merits of this case is whether the 547 patent is invalid on the theory that nizatidine would have been obvious to a person of ordinary skill in the art when it was invented in November 1979. A claimed invention is not patentable if the differences between it and the prior art at the time of the invention "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a); *Graham v. John Deere Co.,* 383 U.S. 1, 13-14 (1966).

The ultimate determination on the issue of obviousness is treated as a question of law, but it is based on factual inquiries that include: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) objective evidence of non-obviousness. *Graham*, 383 U.S. at 17-18; *Yamanouchi Pharmaceutical Co. v. Danbury Pharmacal*, 231 F.3d 1339, 1343 (Fed.Cir.2000); *WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1355 (Fed.Cir.1999).

Such objective evidence may include evidence that the patented invention has enjoyed commercial success, that it met a long-felt but unmet need, that others in the field tried and failed to solve the problem solved by the invention, that the invention produced unexpected and superior results, that others copied the invention, and that others in the industry acquired licenses showing their respect for the invention. *In re Rouffet*, 149 F.3d 1350, 1355 (Fed.Cir.1998); accord, *e.g.*, *Ruiz v. A.B. Chance Co.*, 234 F.3d 654, 662 (Fed.Cir.2000), citing *Graham, supra,* and *Miles Labs., Inc. v. Shandon, Inc.*, 997 F.2d 870, 877 (Fed.Cir.1993); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1555-56 (Fed.Cir.1983).

A patent that has been issue is presumed to be valid. 35 U.S.C. § 282. The party asserting invalidity based on obviousness must prove invalidity by clear and convincing evidence. *E.g.*, *WMS Gaming*, 184 F.3d at 1355; *Lindemann Maschinenfabrik GmbH v. American Hoist and Derrick Co.*, 730 F.2d 1452, 1459 (Fed.Cir.1984) (reversing finding of obviousness).[FN3]

FN3. The Federal Circuit has often said that it may be easier to satisfy the burden if the party asserting invalidity can show that the relevant prior art was not presented to or considered by the patent examiner. *E.g.*, *WMS Gaming*, 184 F.3d at 1355, citing *Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc.*, 98 F.3d 1563, 1569 (Fed.Cir.1996); *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1050 (Fed.Cir.1988). Defendant Zenith has not made such a showing in this case, although it attempted to do so in summary judgment briefing. The prior art compounds upon which Zenith relies here were not only before the examiner, they were described in detail in the 547 patent itself.

Chemical compounds present special issues of obviousness because of the limited number of elements, recurring groups or substituents in complex molecules, the structural similarities within classes of related compounds, and the ability of chemists to undertake systematic experiments modifying known compounds.

***5** In *Yamanouchi,* the Federal Circuit upheld the patent on another of the H2 receptor antagonists-famotidine-against a defense of obviousness. The court explained: "For a chemical compound, a prima facie case of obviousness requires 'structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions.' " 231 F.3d at 1343, quoting *In re Dillon*, 919 F .2d 688, 692 (Fed.Cir.1990) (*en banc*); accord, *In re Papesch*, 315 F.2d 381, 391 (C.C.P.A.1963).

To prevent the distortions of hindsight from invalidating genuine inventions, close attention to the supposed reason or motivation for making the claimed compound is critical. As a leading treatise explains:
Because of the unpredictable nature of chemical reactions, a newly-synthesized compound may be very similar in structure to known and existing compounds and yet exhibit very different properties. Further, many such new compounds are obvious in the sense that any competent chemist could have synthesized them *if requested or motivated to do so.*

2 Donald S. Chisum, Chisum on Patents § 5.04[6] at 5-429 (2000) (emphasis added). In deciding obviousness under § 103(a), the focus is not on the ability of chemists to imagine a compound, nor on their ability to synthesize a molecule to order, but on whether the prior art provided apparent reason or motivation to take the steps that led to synthesis of the new compound. The unpredictable nature of chemical reactions is especially pronounced, of course, when dealing with medicinal chemistry, where the biological effects of chemical reactions may be exceedingly difficult to predict from the chemical structure of a compound.

To show obviousness, the reason or motivation offered by the prior art need not offer "absolute predictability" of the results, but it requires at least a "reasonable expectation of success." *Yamanouchi*, 231 F.3d at 1343, quoting *In re Longi*, 759 F.2d 887, 896 (Fed.Cir.1985); accord, *In re Vaeck*, 947 F.2d

488, 495 (Fed.Cir.1991) (reversing PTO rejection of claims as obvious where prior art offered no "reasonable expectation of success"), citing *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed.Cir.1988).

If the prior art makes a particular experiment or modification only "obvious to try," that does not support a finding of obviousness. See *In re Eli Lilly and Co.*, 902 F.2d 943, 945 (Fed.Cir.1990), citing *In re O'Farrell*, 853 F.2d at 903. The Federal Circuit explained in *O'Farrell* that the "obvious to try" admonition has been directed mainly at two kinds of error. As explained below, one applies here: "In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful." *Id.*

***6** Obviousness cannot be determined by chemical structure alone. As applied to chemical compounds, "a compound and all of its properties are inseparable" and must be considered in determining obviousness. *In re Dillon*, 919 F.2d 688, at 697, citing *In re Papesch*, 315 F.2d at 391; accord, *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 725 (Fed.Cir.1990) (affirming rejection of obviousness defense: "An analysis of obviousness of a claimed combination must include consideration of the results achieved by that combination.").

B. *Zenith's Argument from Structural Similarity*

The first three *Graham* factors address the prior art, the differences between nizatidine and the prior art, and the level of skill in the relevant art.

The obviousness inquiry in this case must focus on the state of the art in late November 1979, when Dr. Pioch invented nizatidine. See 35 U.S.C. § 103(a). Defendant Zenith argues that nizatidine would have been obvious to one skilled in the art of synthetic organic chemistry at that time. Zenith bases this contention on structural similarities between nizatidine and three other H2 receptor antagonists known at that time. Zenith called on Dr. Steven W. Baldwin to explain this defense. Dr. Baldwin is an expert in synthetic organic chemistry and has served for many years as a professor of chemistry at Duke University.

1. *Dr. Baldwin's Analysis*

The analysis begins with the histamine molecule itself. Histamine has the following structure:

[diagram 1]

The diagrams in this entry use certain conventions from organic chemistry. The unidentified angles represent carbon atoms, for which any otherwise unspecified bonds are assumed to be taken up by hydrogen atoms. Thus, the histamine molecule is based on the imidazole ring made up of five atoms-three carbons and two nitrogens. Attached to a carbon atom in the ring is the "side chain."

Dr. Baldwin described the effort to develop an effective H2 receptor antagonist as beginning with the histamine molecule itself, making various modifications to it, and seeing whether those modifications had desirable biological effects. See Tr. 79. The SmithKline French laboratories tried "a huge number of compounds." Some actually promoted gastric acid secretion while others inhibited it. Two early candidates as effective H2 receptor antagonists-burimamide and metiamide-turned out to have problems that precluded their use as safe and effective drugs. After several years of effort, however, the SmithKline French team discovered cimetidine. Like histamine itself, each of those three compounds is based on an imidazole ring, three carbons and two nitrogens. Cimetidine has the following structure:

[diagram 2]

Cimetidine was a breakthrough invention. It launched a revolution in the treatment of peptic ulcers without surgery. It became the number one selling drug in the United States. Its invention was significant enough to figure prominently in the 1988 Nobel Prize for Physiology or Medicine. As noted above, however, cimetidine also produced some undesirable side effects. It also had to be taken four times a day. The SmithKline French team and virtually every major drug company began searching for second-generation H2 receptor antagonists that would be at least as effective as cimetidine but without the side effects.

***7** When Dr. Pioch invented nizatidine in late November 1979, the literature in the field disclosed many thousands of candidate compounds that could be expected to have some level of H2 antagonist

activity. According to Dr. Baldwin, the literature at that time had identified two other compounds that showed the most promise as second generation H2 receptor antagonists: ranitidine and tiotidine. For purposes of discussing Dr. Baldwin's opinion, it is useful to show the structures of cimetidine, ranitidine, and tiotidine together:

[diagram 3]

Ranitidine is built on a furan ring, which has five atoms-four carbons and one oxygen. (Another furan-ring compound, called SKF 93479, has also been tested in humans.) Tiotidine is built on a thiazole ring, which has five atoms-three carbons, one sulfur, and one nitrogen, with one carbon between the sulfur and nitrogen.

As of November 1979, cimetidine was on the market as TAGAMET. Ranitidine was not yet on the market, but it had been disclosed in a patent that had issued on December 5, 1978, for compounds using furan rings that showed H2 antagonist activity. That patent, U.S. Patent No. 4,128,658, disclosed thousands of different furan compounds. Ranitidine is example 15 in the patent, though the name is not used. See Ex. 1075. Tests had shown ranitidine is about four times as potent as cimetidine in terms of its H2 receptor antagonist activity.

Tiotidine was disclosed in U.S. Patent No. 4,165,378, which issued on August 21, 1979. Ex.2054. The 378 patent disclosed guanidine derivatives of imidazoles and thiazoles. The 378 patent also disclosed many compounds with H2 antagonist activity. Tiotidine was example 21. By August 1979, it was public knowledge that tiotidine was undergoing some trials and had been described as "the most potent and selective H2-blocker described to date." Ex.2063 (abstract 635). Later tests with mice showed that tiotidine caused precancerous lesions in the stomach, so the compound was abandoned for therapeutic use. Those effects were not yet known in November 1979. As Judge Owen wrote in *Yamanouchi:* "So much for predictability in the field." 21 F.Supp.2d 366, 372 n. 12 (S.D.N .Y.1998), *aff'd,* 231 F.3d 1339.

Zenith contends that nizatidine was obvious based on Dr. Baldwin's testimony that a synthetic organic chemist of ordinary skill in November 1979 would have recognized that the compound now called nizatidine was part of a special set of just 15 compounds that could be made by mixing and matching segments of cimetidine, ranitidine, and tiotidine. He testified that the hypothetical researcher "would have every reason to expect that these 15 compounds would have H2 receptor antagonist activity." Tr. 109. Dr. Baldwin recognized that the search for second-generation H2 antagonists involved hundreds of thousands of compounds. Tr. 107. However, for purposes of his analysis in this case, he focused on cimetidine, ranitidine, and tiotidine. He explained this focus because cimetidine was already a successful drug and because ranitidine and tiotidine appeared at that time to be the most promising candidates in the development pipeline.

***8** The basis for Dr. Baldwin's opinion is best illustrated visually. He looked at these three successful or promising compounds, and he then divided each into four portions: an aryl side chain, an aryl ring, a connector, and an unsaturated side chain. Dr. Baldwin illustrated the division as follows:

[diagram 4]

In Dr. Baldwin's method, the "connector" segment in all three compounds is identical, while there are three different aryl side chains (one of which is only a hydrogen atom, for cimetidine), three different aryl rings, and two different unsaturated side chains.

Using this division of the three known compounds into these four segments, Dr. Baldwin concluded that a skilled synthetic organic chemist could mix and match those four segments to create 18 different compounds, including the three known compounds. (Without introducing other variables, such as the locations where the chains bond with the rings, there are 18 possible permutations of the three aryl side chains, three aryl rings, one connector, and two unsaturated side chains. 3 x 3 x 1 x 2 = 18.) Dr. Baldwin compared this analysis to picking dishes for separate courses from a restaurant menu.

Nizatidine is the one of the 15 new compounds that uses the dimethyl-aminomethyl group as the aryl side chain, the thiazole ring as the aryl ring, the common connector, and the nitroethylene group as the unsaturated side chain. Nizatidine has the following structure:

[diagram 5]

From this mix-and-match approach, Dr. Baldwin concluded that a researcher of ordinary skill in synthetic organic chemistry who had studied the

public literature on H2 receptor antagonists in November 1979 would have expected all of the 15 compounds to have H2 receptor antagonist activity. Tr. 126. He based that expectation on the common structural features with the three compounds that were known to be H2 receptor antagonists. From that "reasonable expectation," Zenith argues, nizatidine would have been obvious so that the 547 patent is invalid.

2. *The Flaws in Dr. Baldwin's Analysis*

Dr. Baldwin's analysis fails to show that nizatidine was obvious, for structural similarity alone is not sufficient to establish obviousness. *In re Dillon,* 919 F.2d 688, 697 (Fed.Cir.1990) (*en banc*). The party claiming obviousness must show that the prior art provided a reasonable expectation that the particular modification of a prior compound would produce a new compound with the desired properties. That is the premise of *Yamanouchi.* See 231 F.3d at 1345; see also *In re Merck,* 800 F.2d 1091, 1097 (Fed . Cir.1986) (upholding PTO finding of obviousness for claim of new use of already known medication; given close structural similarity and similar psychotropic use of two compounds, one of ordinary skill in the art "would have expected amitriptyline to resemble imiprimaine in the alleviation of depression in humans"). It is not enough, however, to show that it would have been merely "obvious to try" the new invention. *Id.* Dr. Baldwin's analysis fails to meet the test.

***9** First, Dr. Baldwin's analysis considers only whether *some* level of H2 antagonist activity might be expected. The Federal Circuit rejected that approach in the other H2 receptor antagonist case. In *Yamanouchi,* the defendant had argued "that an ordinary medicinal chemist would have reasonably expected the resulting compound to exhibit the baseline level of H2 antagonist activity." 231 F.3d at 1345. The Federal Circuit rejected the argument: "The baseline level of activity is a mere 1/165th the activity of cimetidine. This level of motivation does not show a 'reasonable expectation of success.' " *Id.,* quoting *In re Longi,* 759 F.2d at 897.

Similarly here, Dr. Baldwin conceded that his hypothetical researcher in 1979 could not have predicted from the chemical structures the *levels* of H2 antagonist activity that any of his 15 compounds would be expected to exhibit. Tr. 135. Under the reasoning of *Yamanouchi,* that concession alone defeats Zenith's theory of obviousness.[FN4]

FN4. To avoid this reasoning, Zenith argued in closing that Dr. Baldwin did not phrase his testimony in terms of "baseline" H2 activity. Tr. 568-69. Dr. Baldwin did not ever specify any level of H2 activity that would have been predictable from chemical structure. Zenith's burden is to show obviousness by clear and convincing evidence. It cannot do so by relying on the ambiguity of its own evidence.

Second, Dr. Baldwin's analysis also failed to consider all the other properties of nizatidine that make it a safe and effective drug. Even if the structure of nizatidine alone could have given Dr. Baldwin's hypothetical researcher a reasonable expectation of a high level of H2 antagonist activity, that would still fall far short of what a researcher needed to expect success with a new compound. The hypothetical researcher would have been looking for a compound that showed not only a high level of H2 antagonist activity compared to cimetidine, but also many other critical properties. Those properties would include the absence of dangerous side effects, the ability to be taken orally, the duration of the action (so that the patient need not take pills as often), the absence of toxicity, and a safe therapeutic ratio (the ratio between a lethal dose and a therapeutic dose).

When considering the alleged obviousness of a chemical compound, the compound, its structure, and all its properties are treated as inseparable. *In re Dillon,* 919 F.2d at 697; *In re Papesch,* 315 F.2d at 391. In *Yamanouchi,* the defendant made an obviousness argument that was remarkably similar to Zenith's argument here, which disregards all those other essential properties of the claimed compound. The Federal Circuit emphatically rejected the argument: "The success of discovering famotidine was not discovering one of the tens of thousands of compounds that exhibit baseline H2 antagonist activity. Rather, the success was finding a compound that had high activity, few side effects, and lacked toxicity." 231 F.3d at 1345.

The same reasoning applies here. Dr. Baldwin conceded that his hypothetical researcher would not have had a reasonable expectation that his method of rearranging the segments from cimetidine, ranitidine, and tiotidine would result in a compound having the safety and efficacy needed for FDA approval. Tr. 136. Dr. Baldwin also conceded that "even minor variations to components of an H2 antagonist

chemical structure can have significant effects on biological activity" of the compound. Tr. 170.

***10** Dr. Baldwin's testimony on these points was consistent with the testimony of Dr. Mark Feldman and Dr. Edward C. Taylor, who are both more familiar than Dr. Baldwin is with H2 receptor antagonists and their development, as well as the problems of drug development more generally. [FN5] For example, the different heterocyclic rings that Dr. Baldwin considered-the imidazole ring in cimetidine, the furan ring in ranitidine, and the thiazole ring in nizatidine and tiotidine-have substantially different chemistries that produce unpredictable different biological effects when they are interchanged for one another. See Tr. 319-20.

> FN5. Dr. Feldman is a gastroenterologist who has specialized in treatment of peptic ulcer disease. He has been involved in many clinical trials of H2 receptor antagonists and has written extensively on H2 receptor antagonists, including a major review article in 1990 for the New England Journal of Medicine on H2 receptor antagonists. Dr. Taylor is a medicinal chemist who is now a professor emeritus at Princeton University. Among his many professional publications, he is the editor of "The Chemistry of Heterocyclic Compounds," a treatise of more than 70 volumes on the subject. Over the past 50 years, Dr. Taylor has also been involved in new drug development and has invented a number of drugs and other compounds.

Thus, under the reasoning of *Yamanouchi* and the cases requiring consideration of the properties or results of chemical compounds, Zenith's theory of obviousness falls far short. See also, *e.g.*, *Ortho Pharmaceutical Corp. v. Smith*, 959 F.2d 936, 943 (Fed.Cir.1992) (affirming finding of non-obviousness; "when these compounds were being developed, one could not predict the effect of small structural changes on the biological activity of steroid hormones").

Third, even if structural similarity and some level of H2 antagonist activity were enough, Dr. Baldwin's attempt to demonstrate a reason for trying nizatidine in 1979 depends on artificial constraints and pure hindsight. Dr. Baldwin's conclusion depends on starting only with the three compounds-cimetidine, ranitidine, and tiotidine-and without including any of the other H2 antagonists known in 1979.

If one expands the starting compounds, by including burimamide or metiamide or even a few of the thousands of other H2 antagonists described in the literature by November 1979, the class of candidate compounds quickly expands to a very large number. (For example, the same publication from August 1979 that identified tiotidine as "the most potent and selective H2-blocker described to date" also included just before that abstract two other abstracts that identified other promising H2 receptor antagonists. See Exs.2063 & 2072 and Tr. 199-200.) One could also start with histamine itself, as the SmithKline French group did at the beginning.

Even when the analysis is limited to the three lead compounds, Dr. Baldwin's conclusion also depends on dividing those three lead compounds into exactly four segments-not two, not three, and not five. Dividing them into two or three segments will not produce nizatidine as one of the permutations. See Tr. 158-59. Dividing them into five or more segments produces a much larger class of candidates. For example, the thiazole ring in cimetidine has a methyl group attached to one of the carbons. Dr. Baldwin chose to treat that methyl group as an integral part of the thiazole ring rather than as a fifth segment that could be varied. If the methyl group were treated as a fifth segment that could be treated as present or not present, that one change would have doubled the number of candidate compounds.

As of 1979, no researchers in the field of H2 receptor antagonists were describing their work using the four-segment approach used by Dr. Baldwin. Dr. Baldwin has argued that the published research work showed they were actually using something close to his method, relying in particular on U.S. Patent No. 4,128,658, in which ranitidine is Example 15 (see Ex. 1075) and U.S. Patent No. 4,046,907, which claimed a number of imidazole-based H2 receptor antagonists (see Ex.2056). It appears to the court that the patents Dr. Baldwin relied upon showed that researchers were actually trying a much wider range of variables, dividing the compounds into more than four segments, and generating huge numbers of candidate compounds. Using the actual methods of researchers would have produced (and did produce) a huge number of candidate compounds, from which the selection of nizatidine would not have been at all obvious.

***11** Similarly, even if the hypothetical researcher in 1979 had begun with the three lead compounds but

had also considered their isomers and tautomers-compounds in which the same atoms are arranged in different structures-the number of candidate compounds would have multiplied quickly to a much larger number, from which the selection of nizatidine also would not have been at all obvious. Dr. Baldwin's analysis also did not take into account the so-called steric configurations of the compounds, which multiply the possibilities even more.

Zenith's and Dr. Baldwin's response to these criticisms is to invoke the ghost of William of Ockham, whose famous logical razor praised simplicity in philosophical and scientific explanations.[FN6] Zenith and Dr. Baldwin suggest that there was no need to consider isomers or tautomers or different steric configurations because the promising lead compounds of cimetidine, ranitidine, and tiotidine were so similar in overall structure. Using the lead compounds, they contend, the simplest and most elegant approach, and the natural one to try in the "first pass" at the problem, was the one described by Dr. Baldwin that would have led the ordinary synthetic organic chemist to nizatidine as one of just 15 candidate compounds.

> FN6. William of Ockham was a fourteenth century English Franciscan philosopher. He formulated his "razor" in different ways. One read: *non sunt multiplicanda entia praeter necessitatem*-one should not multiply the number of entities unnecessarily. Applied more broadly, his "razor" declares that a simpler explanation is preferable to a more complex one, all other things being equal.

The court has great respect for the power of Ockham's razor in science, philosophy, and law. In this case, however, Zenith's explanation is pure hindsight. To use the method to produce such a small class of candidate compounds, one must artificially impose the constraints on the number and identity of lead compounds, the number of segments into which they are divided, and the exclusion of other variables such as isomers and tautomers. For a researcher working at the time, choosing exactly the right variables in such a method and analysis would not have been obvious. Just as courts "cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention," *Ecolochem, Inc. v. Southern California Edison Co.*, 227 F.3d 1361, 1371 (Fed.Cir.2000) (internal quotations marks and citation omitted), it is difficult to build a persuasive case of obviousness based on such a methodology that depends on so many arbitrary and artificial constraints to produce the desired result.[FN7]

> FN7. Dr. Baldwin and Zenith contend that the relevant art for this case is synthetic organic chemistry, and that one of "ordinary skill" in that art would have an advanced degree in organic chemistry. Lilly and Dr. Taylor contend that the relevant art for this case is medicinal chemistry and more specifically the development of H2 receptor antagonists. Dr. Taylor testified that one of ordinary skill in that art in 1979 would have been a medicinal chemist with a Ph.D degree in organic chemistry or equivalent training, with two to three years of additional experience in the H2 receptor antagonist field, and would have had an appreciation of the relevant biological events associated with a successful H2 receptor antagonist drug. Tr. 316-17. For purposes of the *Graham* factor regarding the level of ordinary skill in the art, the court finds Lilly's and Dr. Taylor's position more persuasive. The challenge addressed by Dr. Pioch and others in the field was the invention of a safe and effective drug, not merely the creation of a new organic compound with some level of H2 antagonist activity. The work required the researcher to focus on all biological effects of a compound, including those that determine whether the compound will be safe and effective.

To illustrate the use and benefits of hindsight in Zenith's theory of obviousness, the evidence shows that in the late 1970s, hundreds of highly skilled medical chemists working for virtually every major pharmaceutical company in North America, Europe, and Japan were trying to find second generation H2 receptor antagonists. Their employers recognized the huge potential market for such drugs, with annual sales measured in the billions of dollars. They had every incentive to find a new drug that would be more effective and have fewer side effects than cimetidine. Only three succeeded-ranitidine, nizatidine, and famotidine.[FN8] Even the gifted team at SmithKline French, whose development of cimetidine contributed to the Nobel Prize, did not see the solution that Dr. Baldwin and Zenith now describe as so simple. Like *Yamanouchi,* this case

"has all the earmarks of somebody looking at this from hindsight." See 231 F.3d at 1345, quoting 21 F.Supp.2d at 370.

> FN8. Famotidine was not part of Dr. Baldwin's analysis. The invention of famotidine was the subject of litigation in *Yamanouchi,* discussed in detail in this entry. Among the other companies who tried and failed to develop second generation H2 receptor antagonists were Bristol-Myers, Merck, Glaxo, Pfizer, and ICI. Their research identified millions of potential candidate compounds, but none that turned out to be safe, effective, and successful drugs.

C. *Objective Evidence of Non-Obviousness*

***12** Objective evidence of non-obviousness has often been described in judicial opinions as addressing "secondary considerations." The law is clear, however, that such evidence is important and must be considered before a court may find a patent claim invalid for obviousness. *E.g., In re Rouffet,* 149 F.3d at 1355; *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.,* 851 F.2d 1387, 1391 (Fed.Cir.1988) (district court erred in finding obviousness based on prior art but without considering objective evidence of non-obviousness); *Hybritech Inc. v. Monoclonal Antibodies, Inc.,* 802 F.2d 1367, 1380 (Fed.Cir.1986) (objective evidence must be considered before a conclusion on obviousness is reached, and "is not merely 'icing on the cake' ").

Such evidence may be used to rebut a prima facie case of obviousness based on prior art references. In fact, such evidence "may often be the most probative and cogent evidence in the record." *Stratoflex, Inc. v. Aeroquip Corp.,* 713 F.2d 1530, 1538-39 (Fed.Cir.1983). The proponent of the evidence, however, must establish a nexus between the evidence and the merits of the claimed invention. *E.g., In re GPAC, Inc.,* 57 F.3d 1573, 1580 (Fed.Cir.1995); *Demaco Corp.,* 851 F.2d at 1392.

1. *Commercial Success*

From May 1988 through September 2000, Lilly's net sales of nizatidine to wholesalers totaled $3.1 billion, with a yearly peak of $401 million in 1995. Ex. 1012. That is strong evidence of commercial success, especially in a field with three other patented competitors (cimetidine, ranitidine, and famotidine) that had higher levels of sales. Strong evidence of commercial success is not surprising in a case under the Hatch-Waxman Act, of course. If the patented drug were not a commercial success, generic manufacturers would have little interest in offering their own versions of the drug.

Zenith has tried to rebut this evidence by suggesting that the commercial success of nizatidine has no nexus with the invention itself, but resulted instead from effective marketing and advertising. Zenith's argument is not persuasive, and Lilly has met its burden of showing a nexus. First, the only active ingredient in AXID is in fact nizatidine. This is not a case in which a patent claims merely one feature of a more complex commercial product, the success of which may derive from other features. Second, the evidence shows that Lilly's marketing and advertising budgets for AXID (nizatidine) have been relatively modest by industry standards. In addition, although nizatidine sales dropped as the competing brands went off-patent and generics entered the market, AXID has continued to have substantial sales. During 1999, when generic versions of cimetidine and ranitidine were on the market, Lilly still sold $239 million worth of nizatidine. Ex. 1012. In short, the later and continued commercial success of nizatidine offers substantial evidence that the invention was not obvious at the time it was made in 1979.

2. *Unexpected Results*

***13** The Federal Circuit has recognized that unexpected superior results from an invention tend to support a finding that the invention was not obvious to one of ordinary skill in the art. See, *e.g., In re Baxter Travenol Labs.,* 952 F.2d 388, 392 (Fed.Cir.1991); *In re De Blauwe,* 736 F.2d 699, 705 (Fed.Cir.1984).

"The basic principle behind this rule is straight forward-that which would have been surprising to a person of ordinary skill in a particular art would not have been obvious." *In re Mayne,* 104 F .3d 1339, 1343 (Fed.Cir.1997), quoting *In re Soni,* 54 F.3d 746, 750 (Fed.Cir.1995). "The principle applies most often to the less predictable fields, such as chemistry, where minor changes in a product or process may yield substantially different results." *Id.*

The principle may apply especially often when dealing with medicinal chemistry. The biological effects of a new compound will often be too complex

to predict with any accuracy. Experts for both Zenith and Lilly testified that the biological effects of minor changes in the structure of a candidate for an H2 receptor antagonist simply cannot be predicted with any confidence. Their testimony is well supported by the history of challenges and failures in the field.

The evidence in this case also shows that unexpected results played a critical role in the issuance of the 547 patent. The patent examiner initially rejected the claim of nizatidine as obvious based on two prior art references which, when combined, suggested a class of compounds that included the "4,2 isomer" of nizatidine. Ex. 1003 at 92-95; see also *id.* at 98-102 (applicant's attorney's response). Nizatidine is the "2,4 isomer," in which the dimethyl-aminomethyl group is attached to carbon atom 2 in the thiazole ring, and the "connector" is attached to carbon atom 4. In the 4,2 isomer, the bonding positions of the dimethyl-aminomethyl group and the connector are reversed.

In response to this rejection, Dr. Pioch submitted a declaration that showed the results of tests of nizatidine and its 4,2 isomer. Dr. Pioch reported that the 4,2 isomer still shows H2 receptor antagonist activity, but the rates are dramatically lower than the rates for nizatidine itself. Ex. 1003 at 103-04. The examiner relied on these unexpected differences in the level of activity exhibited by the two isomers in allowing the nizatidine claim and issuing the 547 patent. *Id.* at 106-07. Those unexpected results provide substantial objective evidence of non-obviousness.

3. *Long-felt Need and Failure of Others*

The failure of others to develop alternatives to the invention may also be evidence of non-obviousness. *Graham*, 383 U.S. at 17-18; *In re GPAC*, 57 F.3d at 1580. As discussed above, the evidence shows that hundreds of the best medicinal chemists in the world were searching for safe and effective H2 receptor antagonists. After the discovery and initial success of cimetidine, many major pharmaceutical companies all over the world tried to develop improved compounds for the second generation-compounds that would be more effective than cimetidine and have fewer side effects.

***14** As of November 1979, it was too early to know whether anyone else had succeeded. (Ranitidine did not receive FDA approval for use as a safe and effective drug until 1983.) With the benefit of hindsight, it is now clear that although these hundreds of medicinal chemists imagined and tested many thousands of compounds, only three compounds were successful as safe and effective drugs-ranitidine, famotidine, and nizatidine.

The need for improved second-generation H2 receptor antagonists is shown by, among other things, the continued commercial success of nizatidine, ranitidine, and famotidine even after cimetidine went off-patent and cheaper generic versions were available. Physicians with a choice have preferred to use the more expensive second-generation compounds.

In addition, even the SmithKline French team whose development of cimetidine contributed to the Nobel Prize was unable to develop a successful second-generation compound.

This evidence shows that it was very difficult to develop successful alternatives to cimetidine, and it adds support to the conclusion that the 547 patent is not invalid for obviousness.

4. *Copying*

Copying of the patented invention may also provide evidence of non-obviousness. *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 679 (Fed.Cir.1988). Evidence of copying tends to be more compelling in arts in which there is more room to design around patents or to improve upon them. When the invention in question is a drug that has won FDA approval as safe and effective, the incentive to copy is strong. In fact, the ANDA procedures established by the Hatch-Waxman Act require generic drug manufacturers to copy the approved drug. Variations undermine the FDA's ability to assume that if the patented drug is safe and effective, the generic competitor will also be safe and effective.

The fact that copying is likely to be present in many Hatch-Waxman Act cases does not allow the court to ignore the copying as evidence of non-obviousness, even though it may be entitled to relatively little weight. In this case, in this field of new drug design, the very need for copying results from and emphasizes the unpredictability of medicinal chemistry. (As we now know, for example, tiotidine, which plays such a critical role in Dr. Baldwin's structural analysis, later turned out to be toxic.) To gain FDA approval, therefore, a company in Zenith's position must copy the patented invention as closely

as possible. Small changes in chemical structure may have dramatic and unpredictable biological effects. To that extent, the evidence of copying adds a little weight against a finding of obviousness, though it is not essential to this court's ultimate conclusion.

5. *Acquiescence of Others*

Licenses to a patent may be evidence of non-obviousness if they indicate that others in the industry recognize the strength and validity of the patent in question. See *In re GPAC*, 57 F.3d 1573, 1580 (Fed.Cir.1995). Licenses will be entitled to little weight, however, unless the patentee can demonstrate "a nexus between the merits of the invention and the licenses of record." *Id.*, quoting *Stratoflex*, 713 F.2d at 1539. In this case, the licensing is minimal. Lilly made a recent decision to grant an exclusive license to plaintiff Reliant as Lilly shifted its own business efforts in other directions. Such a licensing arrangement does not demonstrate the validity of the patent. The substitution of one business entity for another adds nothing to the overall equation on the issue of obviousness.

D. *Conclusion on Obviousness*

***15** After considering all the evidence on the issue of obviousness, the court concludes that Zenith has failed to show that the 547 patent is invalid for obviousness. Zenith failed to make even a prima facie showing of obviousness based on similar chemical structure. Zenith's analysis (1) failed to account for the inability to predict even the level of H2 antagonist activity; (2) failed to account for the inability to predict the other critical properties that have made nizatidine safe and effective as a drug; and (3) was built with hindsight and artificial constraints.

Under the reasoning of *Yamanouchi*, Lilly was entitled to judgment after Dr. Baldwin conceded that his hypothetical researcher of ordinary skill could not have predicted the level of H2 activity and could not have had a reasonable expectation that nizatidine would be a safe and effective drug. In addition, Lilly has produced substantial objective evidence of non-obviousness. The 547 patent easily withstands Zenith's defense of obviousness under 35 U.S.C. § 103(a). Zenith's ANDA for nizatidine may not be granted on the basis of the Paragraph IV certification asserting invalidity.[FN9]

FN9. *In Yamanouchi*, the district court had entered judgment as a matter of law under Fed.R.Civ.P. 52(c) at the close of the defendant's evidence on obviousness. 231 F.3d at 1342. In this case, Lilly made a similar motion, not only at the end of Zenith's evidence on the question but earlier, in the very midst of Dr. Baldwin's testimony. As a matter of caution, the court did not grant Lilly's motion but took it under advisement so that a complete record could be developed. That more complete record has also been useful in deciding the issue of willfulness. The fact that Lilly's motion was not granted during trial should not be interpreted as an indication that the issue of obviousness was deemed close or difficult.

IV. *Exceptional Case and Willful Infringement*

Zenith's only act of infringement here was filing an amended ANDA with a Paragraph IV certification under the Hatch-Waxman Act. Lilly has shown its patent is valid. Any additional relief for the patentee beyond that declaration would require proof of "commercial manufacture, use, offer to sell, or sale within the United States ... of an approved drug." 35 U.S.C. § 271(e)(4)(C). Lilly contends, however, that the court should find this to be an "exceptional case" under 35 U.S.C. § 285 and award Lilly its attorneys' fees.

Lilly bases its willfulness assertion on the totality of the circumstances, including the weakness of Zenith's invalidity case, Zenith's failure to obtain a written opinion from counsel before the act of infringement, errors and omissions in the written opinion that was provided five weeks after the act of infringement, the inadequacy of Zenith's notice to Lilly of the factual and legal basis of the assertion of invalidity, and Zenith's haste to file its Paragraph IV certification in light of the huge financial gains it might win by being first.

Willful infringement is one form of misconduct that can make a case exceptional for a fee award. *Yamanouchi*, 231 F.3d at 1346-47; *Fromson v. Western Litho Plate and Supply Co.*, 853 F.2d 1568, 1573 (Fed.Cir.1988) (after finding willful infringement, district court erred by failing to explain why it did not award attorneys' fees); *Avia Group Int'l, Inc. v. L.A. Gear California, Inc.*, 853 F.2d 1557, 1567 (Fed.Cir.1988) (finding of willful infringement is sufficient to find case is exceptional). The Hatch-Waxman Act refers to § 285 in 35 U.S.C.

§ 271(e)(4), indicating that Congress plainly anticipated that an ANDA case could justify an award of attorneys' fees. See *Yamanouchi*, 231 F.3d at 1346 (affirming finding of willfulness and fee award). The only ground for finding this case exceptional is willful infringement.

***16** An act of infringement may be deemed willful where the infringer is aware of the patent in question and fails to use due care to avoid infringement. *E.g.*, *Electro Medical Systems, S.A. v. Cooper Life Sciences, Inc.*, 34 F.3d 1048, 1056 (Fed.Cir.1994); *Rolls-Royce Ltd. v. GTE Valeron Corp.*, 800 F.2d 1101, 1109 (Fed.Cir.1986). One statement of the standard is whether the infringer, "acting in good faith and upon due inquiry, had sound reason to believe that it had the right to act in the manner that was found to be infringing. The law of willful infringement does not search for minimally tolerable behavior, but requires prudent, and ethical, legal and commercial actions." *SRI Int'l, Inc. v. Advanced Technology Labs., Inc.*, 127 F.3d 1462, 1465 (Fed.Cir.1997).

As the Federal Circuit recognized in *Yamanouchi*, in ANDA cases involving Paragraph IV certifications challenging the validity of the patent in suit, the alleged infringer will always have been aware of the patent in question. See 231 F.3d at 1347. There is nothing accidental or unintentional about a Paragraph IV certification that claims invalidity. "The joint operation of § § 271(e) and 285 require the paragraph (2) infringer to display care and regard for the strict standards of the Hatch-Waxman Act when challenging patent validity." *Id.* However, the fact that the defendant has filed an ANDA with a Paragraph IV certification and lost a lawsuit on the issue of validity is not enough by itself to support a finding of willful infringement.

The plaintiff alleging willful infringement must come forward with clear and convincing evidence that the defendant failed to exercise due care. *E.g.*, *Comark Communications, Inc. v. Harris Corp.*, 156 F.3d 1182, 1190 (Fed.Cir.1998); *SRI Int'l*, 127 F.3d at 1465. In deciding whether a case is exceptional for these purposes, the court must consider the totality of the circumstances. *Yamanouchi*, 231 F.3d at 1347; *Kaufman Co. v. Lantech, Inc.*, 807 F.2d 970, 978-79 (Fed.Cir.1986).

A. *Advice of Counsel to Rebut Willfulness*

An important factor in deciding willfulness is whether the defendant sought, obtained, and reasonably relied upon competent advice of counsel as to the validity of the patent the defendant intended to challenge. *E.g.*, *Westvaco Corp. v. International Paper Co.*, 991 F.2d 735, 743 (Fed.Cir.1993). The mere fact that an opinion was obtained does not necessarily resolve the issue of willfulness. *E.g.*, *Minnesota Mining and Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1580 (Fed.Cir.1992) (affirming finding of willfulness despite in-house patent counsel's opinion of invalidity).

When an infringer has received an opinion of invalidity from competent counsel before the act of infringement, a finding of willfulness is unusual. However, a court need not take such an opinion at face value. A court presented with an opinion of counsel should review the opinion to determine whether it shows an adequate foundation based on a review of all necessary facts or whether it is merely conclusory. *Westvaco*, 991 F.2d at 743. "Counsel's opinion must be thorough enough, as combined with other factors, to instill a belief in the infringer that a court might reasonably hold the patent is invalid, not infringed, or unenforceable." *Westvaco*, 991 F.2d at 743, quoting *Ortho Pharmaceutical Corp. v. Smith*, 959 F.2d 936, 944 (Fed.Cir.1992). "To serve as exculpatory legal advice the opinion of counsel is viewed objectively, to determine whether it was obtained in a timely manner, whether counsel analyzed the relevant facts and explained the conclusions in light of applicable law, and whether the opinion warranted a reasonable degree of certainty that the infringer had the legal right to conduct the infringing activity." *SRI International*, 127 F.3d at 1467. Also, it is important that the opinion of counsel be obtained before the defendant begins the infringing activity. *E.g.*, *Underwater Devices Inc. v. Morrison-Knudsen Co.*, 717 F.2d 1380, 1389 (Fed.Cir.1983).

B. *The Oral Opinion*

***17** With these standards in mind, the court turns to the evidence on the issue. In 1997, Zenith hired the law firm of Lerner, David, Littenberg, Krumholz and Mentlik ("Lerner David") to evaluate the nizatidine patents, including the 547 patent. On July 11, 1997, Zenith asked Lerner David to order the file histories on the 547 patent and Patent No. 4,760,075 and to determine "whether there is reasonable basis for performing a full invalidity search and opinion on these patents." Ex. 1064. On August 21, 1997, Lerner

David sent Zenith a written analysis of the file histories of the 547 patent and the 075 patent (which is not at issue here). Ex. 1028. The project lay relatively dormant until the summer of 1998. See Exs. 1031, 1035. On July 10, 1998, Zenith directed Lerner David to order an American Chemical Society search on nizatidine. Ex. 1036.

On September 15, 1998, Zenith mailed its ANDA on nizatidine with a Paragraph III certification stating its intention to wait until the 547 patent expired before selling generic nizatidine. In the meantime, Lerner David's billing records show that at least one lawyer spent a good deal of time beginning September 10, 1998, considering the validity of the 547 patent on nizatidine. Ex. 1078. The billing records for September show more than 40 hours of attorney time on the nizatidine project.

The critical day came on October 5, 1998. Three attorneys from Lerner David and two patent attorneys for Zenith held a conference call that lasted about 30 minutes. They discussed the validity of the 547 patent and two other nizatidine patents. The participants from Lerner David were Michael Teschner, Arnold Krumholz, and William Mentlik. The participants for Zenith were Michael Keller and Lee Banks.

Four of the participants testified in depositions about the conference call. (Mentlik was Zenith's lead trial counsel in this action and so was not a witness.) None of the participants testified at trial. The designated deposition testimony indicates that the Lerner David attorneys expressed an opinion that the 547 patent was invalid as obvious and that the Zenith attorneys, Keller and Banks, agreed with that view. Banks volunteered that the oral opinion from Lerner David was "in-depth and complete." Banks Dep. at 232. However, with respect to any details that would have allowed Lilly to probe the actual basis for the opinion, the designated evidence from the four witnesses indicates virtually nothing other than the self-serving bottom line.

It is also surprising and more than a little suspicious that, according to the participants, there were and are no contemporaneous notes or other documents reflecting the content of this critical discussion. Banks testified that his testimony about the telephone call was based on his unaided recollection. Banks Dep. at 238. He had already acknowledged that records had shown his recollection of the relevant events was faulty. *Id.* at 220, 230.

***18** On October 6, 1998, attorneys for Lilly met with Zenith attorney Keller in Florida. The Lilly attorneys disclosed to Keller that no other generic drug manufacturer had filed an ANDA challenging the validity of the 547 patent on nizatidine. That same morning, Keller sent an e-mail to Banks stating: "Lilly was asking questions about this drug. It appears we are first. Brief Eric fully on yesterdays conference call." The reference to "Eric" was to Zenith's Dr. Eric Mittleberg, who did not participate in the telephone conference on October 5, 1998. Dr. Mittleberg was and is Zenith's director of scientific and medical affairs. He made the final decision to file the amended ANDA with the Paragraph IV certification. Later on October 6th, Banks replied to Keller by e-mail: "I have informed Eric of the exact nature of Lerner, David's opinion. Eric wants the amended certification to go in today."

The reference to being "first" is important here, especially in light of Zenith's unusual decision to file the Paragraph IV certification based only on an oral opinion from counsel. Under the Hatch-Waxman Act, the first competitor to file a Paragraph IV certification on a patented drug is entitled (in the absence of a successful suit for infringement) to a 180-day period in which its product will be the only generic competitor. See 21 U.S.C. § 355(j)(5)(B)(iv). Dr. Mittleberg acknowledged that this head-start on other generic competitors is a very lucrative advantage. Industry experience shows that the first competitor tends to be able to keep the lion's share of the business it wins in those first 180 days. Tr. 257-59. At the same time, filing a Paragraph IV certification also has risks. The required notice to the patentee starts a 45-day clock in which the patentee must either surrender the patent's protection or file an infringement suit that is likely to be costly for both sides.

In light of these potential benefits and risks, Zenith's patent attorney Keller wanted to make sure that Dr. Mittleberg was fully aware of the (unspecified) limits of the oral opinion from Lerner David. As Zenith was rushing to prepare the Paragraph IV certification on the afternoon of October 6th, Keller instructed Banks to brief Dr. Mittleberg "fully" on the conference call with Lerner David lawyers. Ex. 1041. Banks did so. Banks also testified that he told Dr. Mittleberg he should call Lerner David's Arnold Krumholz himself to talk about the Lerner David opinion. Banks Dep. at 220-21. There is no evidence from either Dr. Mittleberg or Krumholz that such a call was ever made. See Tr. 278.

Dr. Mittleberg testified at trial. He knows that one of the in-house lawyers told him that Lerner David said the 547 patent was invalid. Dr. Mittleberg did not even remember who told him that, let alone any details of the basis for challenging the patent. Tr. 247. He could not testify about any point except the helpful conclusion-Lerner David and the in-house attorneys had said there was a basis to challenge the patent as invalid. The only witness to testify at trial on the point did not know why or how.

***19** Keller was the patent lawyer for Zenith who was responsible for reaching a conclusion about whether the company had a reasonable basis for concluding that the 547 patent was invalid. Keller Dep. at 54-55, 58-59. The nizatidine ANDA was one of only two cases in which Zenith had filed a Paragraph IV certification based on only an oral opinion from counsel. *Id.* at 167.

Reliance on oral opinions of counsel is not favored. *Minnesota Mining*, 976 F.2d at 1580; *Bott v. Four Star Corp.*, 807 F.2d 1567, 1572 (Fed.Cir.1986), *overruled on other grounds*, *A.C. Aukerman Co. v. R.L. Chaides Const. Co.*, 960 F.2d 1020, 1038-39 (Fed.Cir.1992); *Shiley, Inc. v. Bentley Lab., Inc.*, 601 F.Supp. 964, 968 (C.D.Cal.1985), *aff'd*, 794 F.2d 1561 (Fed.Cir.1986). Oral opinions carry less weight, for example, because they must be proved perhaps years after the event, based only on testimony which may be affected by faded memories and the forces of contemporaneous litigation. *Minnesota Mining*, 976 F.2d at 1580. Nevertheless, reliance on an oral opinion is not necessarily unreasonable as a matter of law. Compare, *e.g.*, *Radio Steel & Mfg. Co. v. MTD Products, Inc.*, 788 F.2d 1554, 1558-59 (Fed.Cir.1986) (affirming finding that infringement was not willful where infringer relied on oral opinion of outside patent counsel), with *American Medical Systems, Inc. v. Medical Engineering Corp.*, 6 F.3d 1523, 1531 (Fed . Cir.1993) (affirming finding of willfulness; oral opinion of invalidity from counsel was not credible, and infringer did not obtain credible written opinion until 20 months after beginning infringement).

The reasons that oral opinions are disfavored are in full view in this case. The exceedingly limited memories of all participants about the details of the oral opinion on October 5th are not credible. The complete and unexplained absence of contemporaneous notes or documents about the oral opinion is suspicious, especially in light of the Zenith's lawyers' need to brief Dr. Mittleberg "fully" on the "exact nature" of the Lerner David oral opinion and its unspecified "limits." Dr. Mittleberg's failure to follow the recommendation to talk directly with attorney Krumholz about the opinion, and Zenith's decision not to call any participants in the October 5th conference call for live testimony at trial, further undermine Zenith's claim that it reasonably relied on a competent opinion of counsel when it filed the Paragraph IV certification on October 6, 1998.[FN10]

FN10. Both parties in this case presented expert testimony on the competence of the Lerner David opinions in this case, both oral and written.

C. *The Later Written Opinion*

Lerner David later provided Zenith with a written opinion, on November 12, 1998. Zenith contends that the later written opinion accurately reflects the substance of the oral opinion given on October 5th. Participants in the October 5th conference call testified to that general point in their depositions, but their memories on all other details of the matter are so limited that the general and self-serving conclusions are not credible. None were called to testify at trial.

***20** In addition, billing records from Lerner David show that extensive work continued on the nizatidine issue after the October 5th conference call, including preparation of a written opinion. See Ex. 1078. On October 6th, Teschner's diary entry was: "Further research regarding the nature of amines and dictation of first rough draft of executive summary opinion." On October 7th, another attorney recorded: "Initial review of validity search results of outside consultant." On October 8th, Teschner recorded: "Review and correction to opinion and begin legal research." Later entries in October indicate a "Dialog search for direct comparison between ranitidine and nizatidine and other H-2 antagonist, review of search results." The work on the written opinion continued in early November. The continuing research and analysis after October 5th were extensive. The apparent need for that later work further undermines Zenith's claim that it relied reasonably on the earlier oral opinion.

On November 12, 1998, Lerner David sent the written letter to Zenith's Lee Banks. The opinion letter described the task: "we have examined whether or not sufficient justification exists for the filing of a certification pursuant to 21 U.S.C. §

355(j)(2)(A)(vii)(IV) (a 'paragraph IV certification') in an Abbreviated New Drug Application ('ANDA') seeking approval to market a generic version of nizatidine." Ex.2045 at 1. The letter offered the following opinion:

As we explained to you in a telephone call on October 5, 1998, having completed our study, we are of the opinion that the three patents in question [including the 547 patent] are invalid. Therefore, in our opinion, the filing of a Paragraph IV certification would comply with the statute. However, as we also advised you, while in our opinion the patents are each invalid, we cannot give you any assurance that you will prevail in challenging the validity of these patents in court.

Id.[FN11]

FN11. The fact that the written opinion did not guarantee victory does not undermine Zenith's ability to rely reasonably upon it. See, *e.g.*, *Westvaco*, 991 F.2d at 744. Also, of course, the fact that a court later disagreed with the opinion does not show that the defendant could not reasonably rely upon the opinion. The issue of willfulness would not even arise unless a court or jury later disagreed with the opinion. See, *e.g.*, *Graco, Inc. v. Binks Mfg. Co.*, 60 F.3d 785, 793-94 (Fed.Cir.1995).

The written opinion letter also included a detailed analysis of the district court decision in *Yamanouchi*. The district court issued the opinion on October 1, 1998, but the Lerner David attorneys did not learn of it until mid-October (apparently October 13th). Diary entries for October show time devoted to analyzing the decision. Because *Yamanouchi* did not figure in the oral opinion on October 5th that Zenith relied upon to undertake the act of infringement, the filing of the Paragraph IV certification, the court has disregarded the later analysis of that case in the written opinion. Based on similar reasoning, the court denied Lilly's earlier motion to compel Zenith to disclose even later advice from its counsel. See *Eli Lilly and Co. v. Zenith Goldline Pharmaceuticals, Inc.*, 149 F.Supp.2d 659, 663 (S.D.Ind.2001).

Even if the court assumed that the November 12th opinion letter accurately reflected the analysis given orally on October 5th, that opinion letter still would not justify reliance upon its conclusions. On first reading by someone not familiar with the issues, the opinion appears to reflect some key indicia of reliability. It discusses prior art, the file history, and one case as a source of the applicable law, and it is from reputable outside patent attorneys.[FN12]

FN12. A court errs if it considers only the qualifications of the attorney involved and fails to consider the competence of the opinion itself. *Jurgens v. CBK, Ltd.*, 80 F.3d 1566, 1572 (Fed.Cir.1996) (reversing and remanding for further consideration after district court declined to follow jury finding of willfulness that necessarily rejected advice of counsel defense).

But upon closer reading-upon the kind of reading that Zenith's own patent attorneys should have given it-several glaring errors of fact and omissions of law come to light. Those errors and omissions weigh heavily against Zenith's claim that it reasonably relied on advice of counsel even if the court were to assume (as Zenith's legal expert did) that the letter accurately stated the basis of the earlier oral advice. Cf. *Yamanouchi*, 231 F.3d at 1347-48 (affirming finding of willfulness where attorney's written opinion contained just one acknowledged error in chemistry that was critical to its conclusion); *Johns Hopkins University v. CellPro, Inc.*, 152 F.3d 1342, 1364 (Fed.Cir.1998) (affirming finding of willfulness where written opinions contained shortcomings and errors that should have been obvious to experienced patent attorney who received them).

***21** The substantive part of the written opinion began with a discussion of the law of obviousness based on structural similarity of two compounds, drawn from *In re Jones*, 958 F.2d 347, 349-50 (Fed.Cir.1992). The letter discussed the Durant patent, No. 4,046,907 (Ex.2056), which disclosed thiazole-based compounds that differed from nizatidine only in the existence and/or identity of a group of atoms bonded to the second carbon in the thiazole ring. For nizatidine, that group is a dimethyl-aminomethyl group.

The opinion acknowledged that Durant did not specifically disclose the use of a dimethyl-aminomethyl group in that position. The opinion stated that Durant did

contemplate the possibility of amino-substituted thiazoles. As is known in the art, the term "amino" is used to describe amines generally and both the

unsubstituted nitrogen found in compound B and the aliphatic amine dimethyl-aminomethyl group found in nizatidine, are amines. Presuming the term "amino" means something other than just a NH2-group, a conclusion which is reasonable in view of certain established nomenclature practices, the use of a dimethyl-aminomethyl group would appear to be contemplated.

Ex.2045 at 5. The opinion went on to state: "it is our opinion that the recitation of 'amino' groups in *Durant* et al. would itself contemplate the use of groups such as the dimethyl-aminomethyl group." *Id.* at 6.

The opinion's treatment of the dimethyl-aminomethyl group as an "amine" or "amino" group was a clear error in chemistry. The evidence at trial from all witnesses on the subject showed a clear and simple difference. An amino or amine group would create a nitrogen-carbon bond with the thiazole ring by bonding a nitrogen atom in the amino or amine group to a carbon atom in the thiazole ring. See, *e.g.*, Tr. 197-98 (Dr. Baldwin); 392-94 (Dr. Taylor). The dimethyl-aminomethyl group in nizatidine creates a carbon-carbon bond between a carbon atom at the base of the group with a carbon atom in the thiazole ring.

The chemical and practical differences between a nitrogen-carbon bond and a carbon-carbon bond are substantial. One skilled in the art would not expect that substituting one for the other would have comparable biological and chemical effects. The erroneous treatment of dimethyl-aminomethyl as having been disclosed by references to amines or amino groups was a basic error that should have been caught by those preparing and reviewing the opinion letter. FN13

> FN13. Zenith's in-house patent attorneys both had backgrounds in chemistry, and they testified that they had others at Zenith review the technical portions of opinions from outside counsel. Banks Dep. at 161-62, 321-22; Keller Dep. at 145.

The opinion letter then made another serious factual error when it addressed the ranitidine patent, No. 4,128,658. The structure of ranitidine differs from that of nizatidine in one major way. The heterocyclic ring for ranitidine is a furan ring (four carbon atoms and one oxygen atom) rather than the thiazole ring in nizatidine. The opinion also noted that U.S. Patent No. 4,239,769 suggested the use of a thiophene ring (four carbon atoms and one sulfur atom). See Ex.2045 at 6.

***22** The opinion letter asserted that one of ordinary skill in the art would have considered both the 658 patent and the 769 patent, and would have found the teaching, suggestion, and motivation to modify those compounds so as to form nizatidine. *Id.* at 7. The opinion letter also discussed a Yellin article comparing cimetidine and tiotidine, as well as a Crenshaw patent, No. 4,374,248.

The opinion letter then offered a different analysis to support its conclusion, based on ranitidine:
Since ranitidine is a commercially successful H-2 antagonist, one of ordinary skill in this area would surely consider various substitutions to potentially improve or modify its efficacy. One substitution which, in our opinion, is suggested by the prior art as a whole and inevitably would be made would be substituting a thiazole ring for the furan ring in ranitidine, as thiazoles already had been shown to be effective as H-2 antagonists.

Id. at 8.

This analysis is based on a fundamental factual error. At the time that nizatidine was discovered in late 1979, ranitidine was not yet a commercially successful H2 antagonist. Ranitidine did not go on the market with FDA approval until 1983. In 1979 it was a promising compound, but its later success was far from obvious in the uncertain world of testing drugs for safety and efficacy (as the later fate of tiotidine also demonstrates). The reference to ranitidine's commercial success was another clear factual error that those who wrote and received the opinion should have caught.

The Lerner David opinion contains a third factual error that is even more important. After discussing the prior art, the authors cautioned that obviousness can be rebutted by a showing of "unexpected and superior results." They wrote: "*While we are currently unaware of any basis upon which Lilly could make such a showing,* * * * if Lilly were able to demonstrate that nizatidine exhibits unexpected results over structurally-related compounds such as those found in *Durant* et al. and/or ranitidine, Lilly might be able to overcome a *prima facie* case of structural obviousness ." *Id.* at 9 (emphasis added).

In fact, Lerner David and Zenith were both aware of such evidence. Lerner David had reviewed the file

history of the 547 patent and had sent an analysis of that history to Zenith on August 21, 1997. See Ex. 1028. As discussed above in terms of the unexpected results of nizatidine, the file history showed that the nizatidine patent claim had initially been rejected as obvious based on certain prior art references. The applicant had overcome that rejection by submitting a declaration from the inventor of nizatidine comparing the H2 antagonist activity of nizatidine and its 4,2 isomer. See Ex. 1003 at 103-04. The result of the change in structure was a marked decrease in H2 receptor activity.

These results showed that nizatidine was unexpectedly superior to its own isomer in terms of H2 antagonist activity. Cf. *In re Mayne*, 104 F.3d 1339, 1343 (Fed.Cir.1997) (affirming PTO finding of obviousness where one isomer was substituted for another: the structural similarity alone suggested functional equivalence). This information about the different properties of the 2,4 and 4,2 isomers was critical to the patent examiner's conclusion to allow the nizatidine claim over the examiner's earlier conclusion of obviousness.

***23** No one should be shocked, of course, if an opinion of invalidity is later undermined by discovery of unexpected results. That uncertainty is inherent in the enterprise, at least if the unexpected results are not part of the file history. But these unexpected and superior results were part of the file history, and Lerner David already knew of them. Lerner David's Arnold Krumholz, who signed the opinion letter, had also sent the analysis of the file history to Zenith. When asked to reconcile this evidence with the opinion letter's statement, Zenith's Banks was unable to do so. Banks Dep. at 308-09. No other evidence explains the discrepancy.

Zenith has tried to minimize this glaring error in the opinion letter by pointing out that the unexpected and superior results in Dr. Pioch's declaration dealt with an isomer of nizatidine and not with ranitidine or other "structurally-related compounds." The effort is not convincing.

The H2 receptor activity is unexpectedly and dramatically different between isomers that have merely interchanged the bonding positions of the two chains to the thiazole ring. Those results cannot be ignored when trying to argue that nizatidine was obvious based on compounds that differed from it even more substantially. Lerner David's review of the file history surely showed that those results were critical to the examiner's decision to issue the patent on nizatidine.

Moreover, it is not as if the opinion letter acknowledged those unexpected and superior results as compared to the 4,2 isomer and then made a reasoned argument as to why they did not undermine a conclusion of obviousness. The Lerner David opinion letter did not even mention this critical evidence weighing against its conclusion on the issue of obviousness. Nor have any witnesses offered any evidence to support the argument that Zenith has offered at trial.

The Lerner David opinion letter has another important omission. It is based entirely on structural similarity between nizatidine and other H2 receptor antagonists. The opinion fails to consider at all the level of H2 antagonist activity or the other properties that make a compound suitable or unsuitable as a medication for human beings. See *Yamanouchi*, 231 F.3d at 1347 (affirming finding of willfulness where ANDA notice of Paragraph IV certification was inadequate because it contained "no reference to famotidine's potency, safety, and lack of side effects, among other distinguishing properties accompanying its unusually high activity").

The court explained above in discussing Dr. Baldwin's analysis why mere structural similarity is not enough by itself to support the obviousness defense. The failure to address the real difficulties and unpredictabilities in this field is further evidence that the opinion was not one that Zenith could reasonably rely upon to support its earlier filing of the Paragraph IV certification. There is no evidence that the authors or readers of the opinion letter thought, let alone reasonably thought, that a hypothetical researcher in 1979 could have predicted from nizatidine's structure the key properties that made it a success. Even at trial, Zenith's expert witness testified that no such predictions could have been made from the structure. The Federal Circuit has written: "A good test that the advice given is genuine and not merely self-serving is whether the asserted defenses are backed up with viable proof during trial which raises substantial questions...." *Read Corp. v. Portec, Inc.*, 970 F.2d 816, 829 n. 9 (Fed.Cir.1992). Zenith's advice fails this test. [FN14]

FN14. Further, it appears that, apart from the Crenshaw patent that did not even surface at trial, the Lerner David opinion was not based on any prior art that was not before the patent examiner. The key compounds

> upon which the opinion and Zenith's trial presentation relied-cimetidine, tiotidine, and ranitidine-were all before the examiner and are discussed in the 547 patent itself. In one of its first decisions on advice of counsel, the Federal Circuit affirmed a finding of willfulness in the face of similar advice. Noting that 35 U.S.C. § 282 assigns a burden that is "most formidable when the party asserting invalidity relies upon prior art considered by" the PTO, the court concluded: "In short, the attorney's advice, based solely on file history prior art, *does not by itself* raise an inference of good faith substantial enough to convince us that the trial court's determination of willful infringement was clearly erroneous." *Central Soya Co. v. George A. Hormel & Co.*, 723 F.2d 1573, 1577 (Fed.Cir.1983) (emphasis in original); accord, *SRI International*, 127 F.3d at 1466 (affirming finding of willfulness where counsel's opinion simply repeated arguments that had been rejected on re-examination).

***24** The Lerner David opinion letter reflects yet another serious omission. As discussed above, the evidence on the objective indicia of non-obviousness weighs substantially against a finding of obviousness in this case. Apart from the erroneous claim that the authors were unaware of any evidence of unexpected results, the opinion included no discussion at all of the objective indicia of non-obviousness or the possibility that such evidence might rebut a prima facie case of obviousness.

In a case arising from a Paragraph IV certification under the Hatch-Waxman Act, certain objective indicia are likely to be present. As discussed above, commercial success and copying will probably be present. Evidence of long-felt need and the failure of others may not always be present in Hatch-Waxman Act cases, but the possibility of such evidence surely must be considered in any reasonable evaluation of obviousness.

To try to explain the failure to mention these objective indicia, Zenith points out that the authors and the recipients were all patent lawyers and did not need to be reminded about these well-known points. As applied to these fact-sensitive factors that directly affect the determination, the explanation is not persuasive. See, *e.g., In re Hayes Microcomputer Products Patent Litigation,* 982 F.2d at 1543 (affirming finding of willfulness despite counsel's opinion that claims were obvious; letter failed, among other points, to consider "secondary considerations in determining obviousness"); see also *Johns Hopkins University v. CellPro, Inc.*, 152 F.3d 1342, 1364 (Fed.Cir.1998) (affirming finding of willfulness; opinion letters mentioning inequitable conduct made no mention of necessary "intent to deceive," which is "often difficult to establish"); *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566, 1571 (Fed.Cir.1996) (counsel's opinion was flawed because it made "no mention of Aerosonic's copying and other objective indicia of unobviousness, although precedent requires that these factors be considered," but appellate court affirmed trial court finding of no willfulness based on totality of evidence and deferential review of factual finding). In addition, Zenith has not offered any evidence at all that any of the lawyers involved in the conference call or in writing or reading the opinion letter ever gave any actual consideration to those objective indicia of non-obviousness. Their failure to do so further undermines the ability of Zenith to rely on advice of counsel as a defense.[FN15]

> FN15. Lilly also points out that the Lerner David opinion letter failed to address the burden of proof on the issue of obviousness. The burden of proof requires a party challenging a patent's validity for obviousness to produce clear and convincing evidence to overcome the statutory presumption that a patent is valid. *E.g., WMS Gaming*, 184 F.3d at 1355. Zenith explains the silence on the issue of the burden of proof as having been unnecessary in an opinion letter from one group of patent attorneys to another. The burden of proof is well-known, simple, and general. The court finds Zenith's explanation is plausible as to that rule of black-letter law.

A further factor showing this is an exceptional case is the inadequacy of Zenith's notice under the Hatch-Waxman Act. Zenith was required to notify Lilly that Zenith had filed its ANDA asserting that the 547 patent is invalid. Such a notice "shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid...." 21 U.S.C. § 355(j)(2)(B)(ii).

In *Yamanouchi,* one important factor supporting the Federal Circuit's decision to affirm a finding of willfulness was the failure of the defendant's ANDA notice to satisfy this requirement. The defendant's

notice "does not present a *prima facie* case of invalidity, and makes no reference to famotidine's potency, safety, and lack of side effects, among other distinguishing properties accompanying its unusually high activity." 231 F.3d at 1347. The Federal Circuit even emphasized the testimony from the defendant's expert witness that was strikingly similar to Dr. Baldwin's testimony here: "Moreover, Dr. Loev admitted at trial that, as of 1992, he could not tell from [famotidine's] chemical structure whether it would be toxic nor predict its lack of side effects. He further testified that he could not predict the effects on potency that would be caused by the structural manipulations he claimed to be obvious." *Id.*, quoting *Yamanouchi*, 21 F.Supp.2d at 376. The Federal Circuit then said: "When Danbury proceeded in the face of these weaknesses, its certification amounted to baseless and unjustified misconduct. In certifying invalidity, Danbury disregarded its duty to exercise due care." 231 F.3d at 1347.

***25** In light of Dr. Baldwin's concession that he also could not predict nizatidine's level of activity, its lack of toxicity, or the lack of serious side effects from its structure, precisely the same reasoning applies here. Zenith's notice to Lilly of the ANDA Paragraph IV certification is as inadequate as Danbury's notice was in *Yamanouchi*. Zenith's notice to Lilly, which was drafted by Lerner David, cited five publications from prior art and stated its conclusion in two sentences: "The composition of matter, nizatidine, is highly structurally similar to compounds disclosed in *Durant* et al., *Crenshaw* et al. and to ranitidine, and any differences therebetween are suggested by the prior art. In addition, the properties resulting from both ranitidine and nizatidine are highly analogous." Ex. 1070. That's it. That does not come close to "a detailed statement of the factual and legal basis" of the assertion of invalidity.

In sum, the evidence here shows clearly and convincingly that Zenith's infringement of the 547 patent was willful. Zenith knew of Lilly's patent, of course, and it knew that its proposed product would infringe the 547 patent. That much will be present in any Paragraph IV cases under the Hatch-Waxman Act. Most important, the evidence shows clearly and convincingly that Zenith did not rely reasonably and in good faith on the advice of counsel. Zenith did not have a reasonable basis for believing the 547 patent was invalid.

Zenith rushed to file its Paragraph IV certification as quickly as possible on the basis of a hurried oral opinion that no participants can describe so as to give anyone confidence that sufficient care had been taken. The financial incentives to file immediately were great, as Zenith noted at the time. Those involved in the October 5th conference call knew that the opinion was highly likely to result in expensive litigation, but also that the potential rewards of success would be measured in many millions of dollars. Yet no one in that conference call testified to any content beyond the bare bottom line. No one in that conference call jotted down even a single note, despite the concern about the "exact nature" of the opinion and its unspecified limits. Dr. Mittleberg failed to follow Zenith's own lawyer's advice to talk directly with Lerner David's Krumholz about the validity issue.

Even when Lerner David took more than a month to clean up the oral opinion by preparing a written opinion, the opinion letter contained glaring errors and omissions that both the authors and the recipients should have recognized. See, *e.g.*, *Johns Hopkins University v. CellPro*, 152 F.3d at 1364 (recipient of opinion letters was experienced patent attorney and should have recognized obvious shortcomings of counsel's opinions). Those errors and omissions had the cumulative effect of thoroughly undermining the reliability of the conclusion of obviousness.

The court recognizes that reasonable and good faith challenges to the validity of patents are an essential part of the patent law system:
***26** A party who has obtained advice of competent counsel, or otherwise acquired a basis for a *bona fide* belief that a patent is invalid, can be said to serve the patent system in challenging that patent in a law suit conducted fairly, honestly, and in good faith. Such a party should not have increased damages or attorney fees imposed solely because a court subsequently holds that belief unfounded, particularly when the issues may be fairly described as "close."

Kloster Speedsteel AB v. Crucible, Inc., 793 F.2d 1565, 1581 (Fed.Cir.1986). The Paragraph IV provision of the Hatch-Waxman Act also invites challenges to drug patents, so long as the challenges are reasonable and in good faith.

This case, however, does not present a close question on the issue of validity. Zenith was not relying reasonably and in good faith on advice of counsel when it decided to go forward with the act infringing the 547 patent. The evidence shows clearly and convincingly that Zenith and its lawyers were going through the motions of preparing an advice of counsel defense. "The evidence shows that the advice

of counsel was more of a protective device than a genuine effort to determine before infringing whether the patent was invalid." *In re Hayes Microcomputer Products Patent Litigation,* 982 F.2d at 1544 (affirming finding of willful infringement despite advice of counsel that patent was invalid). This is an exceptional case for purposes of 35 U.S.C. § 285, and Lilly is entitled to recover its attorneys' fees.

Conclusion

For the reasons detailed in this entry, the court finds that U.S. Patent No. 4,375,547 is not invalid as obvious under 35 U.S.C. § 103(a). The court further finds that Zenith's act of infringement was willful, made without exercising due care, and that this case is an exceptional case under 35 U.S.C. § 285. The court postponed taking evidence on the amount of any fee award until it was determined whether a fee award would be appropriate. Unless the parties agree or the court later orders otherwise, Lilly shall submit a detailed written fee petition no later than November 30, 2001. (Plaintiff Reliant, which voluntarily joined in this suit earlier this year after signing a license agreement with Lilly, is not entitled to its own fee award.) Zenith shall submit any response no later than January 15, 2002. Lilly may file any reply no later than January 31, 2002. The court will schedule an evidentiary hearing or oral argument on written request, but will otherwise rule based on the written submissions.

So ordered.

S.D.Ind.,2001.
Eli Lilly & Co. v. Zenith Goldline Pharmaceuticals, Inc.
Not Reported in F.Supp.2d, 2001 WL 1397304 (S.D.Ind.)

Briefs and Other Related Documents (Back to top)

- 2001 WL 34887767 () Expert Report of Steven Worth Baldwin, Ph.D. (Oct. 12, 2001) Original Image of this Document (PDF)
- 2001 WL 34888835 (Trial Motion, Memorandum and Affidavit) Plaintiffs' Motion in Limine to Preclude Testimony from Dr. Steven Baldwin Relating to the Pharmacology & Physiology of Gastric Acid Secretion and the H2 Receptor (Sep. 10, 2001) Original Image of this Document (PDF)
- 2001 WL 34888838 (Trial Motion, Memorandum and Affidavit) Plaintiff Eli Lilly and Company's Motion Pursuant to Fed. R. Civ. P. 52(C) for Partial Judgment as A Matter of Law that the '547 Patent is not Invalid (Sep. 10, 2001) Original Image of this Document (PDF)
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- 2001 WL 34888837 (Trial Motion, Memorandum and Affidavit) Lilly's First Motion in Limine to Preclude Testimony from Dr. Steven Baldwin on his Four-Part Analysis of the Structure of Three Selected H2-Receptor Antagonists (Aug. 27, 2001) Original Image of this Document (PDF)
- 2001 WL 34888840 (Trial Motion, Memorandum and Affidavit) Defendant's Memorandum in Support of its Motion in Limine to Exclude the Second Expert Report and Portions of the First Expert Report of Harry F. Manbeck, Jr. and Corresponding Testimony (Aug. 27, 2001) Original Image of this Document (PDF)
- 2001 WL 34888839 (Trial Motion, Memorandum and Affidavit) Memorandum of Defendant Zenith Goldline Pharmaceuticals, Inc. in Opposition to Plaintiffs' Motion for Partial Summary Judgment (Aug. 8, 2001) Original Image of this Document (PDF)
- 2001 WL 34887765 () Second Expert Report of Harry F. Manbeck, Jr. (Jul. 17, 2001) Original Image of this Document (PDF)
- 2001 WL 34887789 () Expert Report of Edward C. Taylor, Ph.D. (Jul. 17, 2001) Original Image of this Document (PDF)
- 2001 WL 34887763 () Deposition of Steven Baldwin, Ph.D. (Jun. 7, 2001) Original Image of this Document (PDF)
- 2001 WL 34887764 () Expert Report of Harry F. Manbeck, Jr. (May 2, 2001) Original Image of this Document (PDF)
- 2001 WL 34888834 (Trial Pleading) Second Amended Complaint (Mar. 7, 2001) Original Image of this Document (PDF)
- 1999 WL 33996967 () Expert Report of Steven Worth Baldwin, Ph.D. (1999) Original Image of this Document with Appendix (PDF)

END OF DOCUMENT

UNREPORTED CASES

Takeda Chem. Indus., Ltd. v. Mylan Labs, Inc.,
Nos. 03-8253, 04-1966, 2006 WL 2686779
(S.D.N.Y. Sept. 20, 2006)

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Slip Copy, 2006 WL 2686779 (S.D.N.Y.)
(Cite as: Slip Copy)

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Briefs and Other Related Documents

Takeda Chemical Industries, Ltd. v. Mylan Laboratories, Inc.S.D.N.Y.,2006.Only the Westlaw citation is currently available.

United States District Court,S.D. New York.

TAKEDA CHEMICAL INDUSTRIES, LTD. and **Takeda** Pharmaceuticals North America, Inc., Plaintiffs,

v.

MYLAN LABORATORIES, INC., Mylan Pharmaceuticals, Inc., and UDL Laboratories, Inc., Defendants.

Takeda Chemical Industries, LTD. and **Takeda** Pharmaceuticals North America, Inc., Plaintiffs,

v.

Alphapharm PTY. LTD. and Genpharm, Inc., Defendants.

Nos. 03 CIV. 8253(DLC), 04 CIV.1966.

Sept. 20, 2006.

Anthony J. Viola, Andre K. Cizmarik, Edwards Angell Palmer & Dodge LLP, New York, NY, and David G. Conlin, Barbara L. Moore, Kathleen B. Carr, Edwards Angell Palmer & Dodge LLP, Boston, MA, for Plaintiffs.

Edgar H. Haug, Kevin F. Murphy, Jeffrey A. Hovden, Frommer Lawrence & Haug LLP, New York, NY, for Defendants Alphapharm Pty. Ltd. and Genpharm, Inc.

Martin B. Pavane, Edward V. Di Lello, Mindy H. Chettih, James P. Doyle, Cohen, Pontani, Lieberman & Pavane, New York, NY, for Defendants Mylan Laboratories, Inc., Mylan Pharmaceuticals, Inc., and UDL Laboratories, Inc.

OPINION & ORDER

DENISE COTE, District Judge.

***1** On March 10, 2006, judgment was entered following a non-jury trial in favor of plaintiff and patentee Takeda Pharmaceutical Company, Ltd. (formerly Takeda Chemical Industries, Ltd.), and its affiliate Takeda Pharmaceuticals North America, Inc. (collectively, "Takeda") and against two generic drug companies, Alphapharm Pty. Ltd. and Genpharm, Inc. (collectively, "Alphapharm") and Mylan Laboratories, Inc., Mylan Pharmaceuticals, Inc., and UDL Laboratories, Inc. (collectively, "Mylan"), in connection with the latters' challenges brought under the Hatch-Waxman Act to Takeda's U .S. Patent No. 4,687,777 (" 777 Patent"), which protects the invention of the chemical compound known as pioglitazone. *Takeda Chemical Industries, Ltd. v. Mylan Laboratories, Inc.*, 417 F.Supp.2d 341 (S.D.N.Y.2006) ("Opinion"). Pioglitazone is a highly successful drug used in the treatment of diabetes.

Takeda has now moved for an award of attorneys' fees against both defendants, arguing that this is an exceptional case. Takeda contends that each of the defendants lacked a good faith basis for its Hatch-Waxman Act Paragraph IV certification and engaged in litigation misconduct. Takeda's motion is granted. FN1

FN1. The Opinion mistakenly described Howard Rosenberg as one of Alphapharm's trial experts. Opinion at 381 n. 64. Howard Rosenberg was a fact witness for Alphapharm. Mylan served Michael Rosenberg's expert report, but before trial withdrew its proffer of him as an expert. The Opinion also erred when, in a moment of unintentional literary homage, it identified Alphapharm's expert Brian Wright, a Professor of Economics at the University of California at Berkeley, as Richard Wright. *Id.* at 345.

An award of attorneys' fees should not be made without a careful consideration of the litigation as a whole and the parties' arguments. The framework established by Congress for accelerating the approval process for generic versions of established drugs, however, is not an invitation to frivolous, bad faith attacks on patents.

As described in considerable detail below, Takeda has shown by clear and convincing evidence that Alphapharm and Mylan each filed baseless Paragraph IV certifications attacking the validity of the 777 Patent. Alphapharm's certification, which asserted invalidity due to obviousness, was deeply flawed and Alphapharm revised its theory again and again in a futile effort to state a prima facie case of obviousness. Mylan completely abandoned its Paragraph IV theory of invalidity and proceeded to trial on a contorted claim that Takeda had engaged in inequitable conduct before the Patent and Trademark

Office ("PTO"). Beyond their baseless certifications, Alphapharm and Mylan each engaged in other litigation misconduct. Their misconduct was exceptional and fully justifies the award of attorneys' fees.

Legal Standard

By operation of law, Alphapharm and Mylan each infringed Takeda's patent by filing an Abbreviated New Drug Application ("ANDA") to make a generic form of pioglitazone before the expiration of Takeda's 777 Patent. 35 U.S.C. § 271(e)(2). An ANDA announces the intention of the filer to produce a bioequivalent form of a drug already approved by the FDA. When filing the ANDA the applicant must make a certification regarding any patent protecting the drug that will be copied. Both Alphapharm and Mylan chose to make a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii) ("Paragraph IV"), certifying that the patent protecting pioglitazone was invalid. In making the certification, Alphapharm and Mylan were required to give Takeda notice of the " 'factual and legal basis' of invalidity." *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1347 (Fed.Cir.2000) (citing to 21 U.S.C. § 355(j)(2)(B)(ii)).

***2** An ANDA filer must "display care and regard for the strict standards of the Hatch-Waxman Act when challenging patent validity." *Id.* Such challenges are only authorized under the Hatch-Waxman Act "in accordance with strict statutory requirements" and require the challenger to state in the Paragraph IV certification that "in the opinion of the applicant *and to the best of his knowledge,* that each patent for which the applicant is seeking approval is invalid." *Id.* (citation omitted). ANDA filers are thus held to a "duty of due care" under the Hatch-Waxman Act. *Id.*

Among the remedies that are available when a patent is infringed by the filing of an ANDA is an award of attorneys' fees under 35 U.S .C. § 285 ("Section 285"), which allows the award of attorneys' fees to the prevailing party in "exceptional cases." *Id.* at § 271(e)(4). The determination of whether a case is exceptional is made by looking at the "totality of the circumstances." *Yamanouchi*, 231 F.3d at 1347 (citation omitted). In order to justify an attorneys' fees award the evidence that the case is exceptional must be "clear and convincing." *Interspiro USA, Inc. v. Figgie Intern. Inc.*, 18 F.3d 927, 933 (Fed.Cir.1994). If a case is determined to be exceptional, the decision to grant attorneys' fees is not automatic; an award should only be made when it is separately determined that it is warranted. *Id.*

Litigation misconduct that may support an "exceptional case" finding under Section 285 includes "vexatious or unjustified litigation or frivolous filings." *Glaxo Group Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1350 (Fed.Cir.2004). For example, cases that arise from the filing of an ANDA may become exceptional for purposes of Section 285 "if the ANDA filer makes baseless certifications." *Yamanouchi*, 231 F.3d at 1347; *see also Glaxo Group*, 376 F.3d at 1351 (noting that "baseless accusations of invalidity" permit an award of attorneys' fees against ANDA filers). A baseless certification includes the failure "to present even a prima facie case of invalidity in filing [the] paragraph IV certification." *Glaxo Group*, 376 F.3d at 1350. The Federal Circuit has cautioned, however, that "the *mere fact that a company has filed an ANDA application or certification* cannot support a finding of willful infringement for purposes of awarding attorney's fees." *Id.* at 1350-51 (emphasis supplied). Filing a baseless Paragraph IV certification and proceeding to challenge a patent's validity despite glaring weaknesses in the theory of invalidity constitute litigation misconduct. *Id.* at 1350. Where a non-prevailing party has pursued litigation in good faith, an award of attorneys' fees is only warranted where that party has engaged in misconduct in the litigation. *See Brooks Furniture Mfg ., Inc. v. Dutailier Intern. Inc.*, 393 F.3d 1378, 1381 (Fed.Cir.2005); *Forest Labs., Inc. v. Abbott Labs.*, 339 F.3d 1324, 1328-29 (Fed.Cir.2003).

***3** Takeda's motion for an award of attorneys' fees from Alphapharm will be addressed first. This ruling presumes familiarity with the Opinion, which contains the findings of fact and conclusions of law following trial and which is incorporated by reference. Nonetheless, various terms, references and findings which are set out in detail in the Opinion are on occasion also briefly described here.

Discussion

I. Alphapharm

A. Reliance on Advice of Counsel

Before discussing the merits of the motion addressed to Alphapharm, it is necessary to determine whether

Alphapharm may oppose this motion by relying on two opinions of counsel that it first produced to Takeda on April 28, 2006, with its opposition to this motion. For several reasons, it may not.

One of the opinions Alphapharm produced is a letter/memorandum dated July 12, 2003, and signed by Allen Kipnes ("Kipnes"), an attorney with the law firm Watov and Kipnes. Frommer Lawrence & Haug LLP ("Frommer"), Alphapharm' s outside counsel, retained Kipnes at the request of Generics [UK], an Alphapharm affiliate, to prepare a legal opinion regarding the validity of the 777 Patent. Kipnes reported that he and medicinal chemist Dr. Edward Glamkowski, with whom Kipnes consulted in preparing his opinion, had concluded that Takeda's previous disclosure of the six-methyl compound, which is referred to as compound (b) in the Opinion and here, in both an earlier patent issued to Takeda and in an article in a scientific journal, rendered pioglitazone obvious. The prior art patent discussed by Kipnes is U.S. Patent No. 4,287,200 (" 200 Patent") and the scientific article is T. Sohda et al., *Studies on Antidiabetic Agents. II. Synthesis of 5-[4-(1-Methylcyclohexylmethoxy)-benzyl]) thiazolidine-2,4-dione (ADD-3878) and its Derivatives,* Chem. Pharm. Bull., 30:3580-3600 (1982) ("Sohda II"). Kipnes noted that the 200 Patent was a "broad disclosure of the claims compounds" and that Sohda II was a more specific disclosure in which compound (b) was shown to be "among a group that showed potent activity but considerable increases in body weight and fat." Kipnes took the view that based on the two disclosures, the patent examiner "should have rejected the claims of the application on prior art grounds." At trial, Alphapharm argued that the disclosure of compound (b) in these two pieces of prior art rendered pioglitazone obvious. Specifically, it asserted that the prior art identified compound (b) as a "lead" compound whose investigation would have led to the discovery of pioglitazone.

Kipnes also opined that the differences in toxicity to the liver and heart reported in Table 1 of the 777 Patent between pioglitazone and compound (b) were not surprising, and therefore were insufficient to overcome pioglitazone's prima facie obviousness. *See* Opinion at 360-62 (describing Table 1). Primarily, Kipnes questioned whether the differences between pioglitazone and the other compounds reported in Table 1 were "material" and also suggested that those reported results contradicted statements made in the 200 Patent and Sohda II.

*4 The second opinion Alphapharm recently produced came from Frommer attorney Jeffrey Hovden ("Hovden"). Hovden indicated that, following receipt of the Kipnes opinion, a synthetic organic chemist Dr. Ali Berkin ("Berkin"), employed by Frommer, prepared Alphapharm's Section 355 Statement under Hovden's supervision. *See* Opinion at 366-67(describing Alphapharm's Section 355 Statement).

Alphapharm was required to disclose any reliance it wished to assert in this lawsuit on advice of counsel by July 30, 2004. Because it did not disclose at that time its intent to rely on an advice of counsel defense in opposing an award of attorneys' fees to Takeda, it may not do so now.

Takeda made no secret that it would move for an award of attorneys' fees in this case. Takeda's complaint explicitly sought an award of attorneys' fees based on a finding that this case is exceptional under 35 U.S.C. § 285. On February 11, 2004, Takeda wrote to warn Alphapharm that its Paragraph IV certification, which had been filed just two weeks earlier, on January 29, 2004, appeared to have "serious omissions and errors." As explained at a conference of July 16, 2004, and as reflected in a Scheduling Order of July 20, 2004 ("July 20 Order"), the defendants' motions to bifurcate discovery and postpone their identification of and discovery concerning any advice of counsel defense were denied due to concerns regarding efficiency, expense, and prejudice.[FN2] Because the defendants had not yet identified with any clarity the issues as to which they might interpose such a defense, they were required to identify the issues on which they intended to assert an advice of counsel defense by July 30. Following such a disclosure, Takeda could demand production of documents withheld because of an assertion of privilege and take appropriate discovery. On July 30, Alphapharm notified Takeda that it would rely on advice of counsel as to the combination use patent issues only. [FN3]

FN2. Alphapharm noted at the July 16 conference that it wished to preserve its right to take an interlocutory appeal from the Order, but filed no such appeal.

FN3. Alphapharm later retracted that notice, and decided not to waive the privilege even as to the combination use patents. The combination use patents are for the use of pioglitazone in combination with other therapies. *See* Takeda Chem. Indus., Ltd. v.

Watson Pharms., Inc., 329 F.Supp.2d. 394, 398-99 (S.D.N.Y.2004).

Alphapharm also forfeited any right to rely on the Kipnes opinion when it did not identify the document on a privilege log or otherwise in response to Takeda's June 2, 2004 request for production of documents. The request included a demand for all documents concerning any opinion or advice of counsel sought or obtained by the defendants concerning the validity of the 777 Patent. Alphapharm has not given any excuse for this omission. Such an omission is wrongful, and provides an independent basis for the suppression of the Kipnes opinion.

Essentially, Alphapharm made a unilateral decision to disregard the July 20 Order and its discovery obligations, and to grant itself a bifurcation of discovery. Alphapharm's conduct is vexatious and constitutes litigation misconduct.

Of course, the very concerns about delay, expense and prejudice which underlay the decision to deny the motions for bifurcation are resurrected by Alphapharm's attempt at this late date to reopen discovery. Even now, Alphapharm has made only the most limited and piecemeal disclosure of its privileged documents. Takeda would not be required to take this limited production at face value, but would be entitled to disclosure of all relevant documents and an opportunity to depose witnesses to test the bona fides of this reliance defense.[FN4]

FN4. For reasons it is unnecessary to describe here, the Kipnes opinion is deeply flawed and Takeda would have been to entitled to show that Alphapharm was well aware of that fact. Based on just the Kipnes opinion and Hovden declaration, Takeda asserts that it would have taken at least five additional depositions if the material had been produced as required in 2004.

***5** Alphapharm asserts that the Court's decision in January of this year, on the eve of trial summations, to take separate briefing on the issue of attorneys' fees following a ruling on the merits of the challenges to the 777 Patent was a decision to bifurcate discovery on the attorneys' fees issue. This argument is frivolous.[FN5] The briefing schedule for the attorneys' fees motion in 2006 did not vacate the July 2004 Order that discovery would not be bifurcated, and Alphapharm has pointed to nothing that was said during the trial that could lead to a good faith belief that discovery would be reopened. Indeed, the motion papers filed by Alphapharm's co-defendant Mylan in opposition to this motion for an award of attorneys' fees recognizes, as they must, that Mylan cannot rely on any advice of counsel it previously received but did not disclose in 2004.

FN5. Alphapharm's similar argument that in July 2004, the Court "carved out the § 285 issues" is entirely specious. At the July 16 conference, the Court noted that the parties had been unclear on which issues they might assert an advice of counsel defense, and therefore ordered them to give notice by July 30 of every issue on which they intended to assert the defense. In giving this ruling, the Court noted that it would need a lot more information to make a judgment about efficiency and duplication of effort issues that would accompany any bifurcation, if the only issue to which the defense was relevant was the issue of attorneys' fees. Because the defendants never indicated that the only relevant issue was their defense to a demand for attorneys' fees, and never presented the additional information necessary to support their bifurcation motion, there was no basis to bifurcate and no bifurcation even as to attorneys' fees.

The Kipnes opinion has, in any event, very little relevance to either prong of Takeda's motion. It was obtained at least nineteen months after Alphapharm made its decision to file its Paragraph IV certification. As reported by Alphapharm, that decision had been made by November 2, 2001, at the latest; it did not obtain the Kipnes opinion until July 2003.

Similarly, Alphapharm is not in a position to rely on any work done by Berkin. Berkin is a synthetic organic chemist, and Alphapharm moved at trial, successfully, to strike the testimony of Takeda expert Dr. James Hendrickson on the ground that a synthetic organic chemist is not qualified to opine on the selection of a lead compound for further pharmacological development. *Takeda Chem. Indus. v. Mylan Labs., Inc.*, 03 Civ. 8253(DLC), 2006 WL 83366 (S.D .N.Y. Jan. 11, 2006). As described in the Opinion, demonstrating that it would be obvious to select compound (b) as a lead compound was critical to Alphapharm's argument that the 777 Patent was

invalid.[FN6] *See* Opinion at 375-80.

FN6. Alphapharm used the same argument in its effort to exclude testimony from Takeda expert Dr. Samuel Danishefsky. *See* Opinion at 373. The Court found that he was superbly qualified to opine in the field of medicinal chemistry. *Id.*

In sum, Alphapharm may not interpose an advice of counsel defense on the motion for an award of attorneys' fees. Indeed, its contention that it is entitled to do so is frivolous and vexatious.

B. Alphapharm's Paragraph IV Certification

Takeda contends that Alphapharm's January 29, 2004 Section 355 Statement was devoid of merit. Even as described in the Opinion, the Statement contained clear errors as well as arguments that Alphapharm abandoned by the time of trial. Opinion at 366-67. Viewed in its totality, Alphapharm's Section 355 Statement is so devoid of merit and so completely fails to establish a prima facie case of invalidity that it must be described as "baseless." When viewed in the context of the totality of this litigation, the filing strongly supports an award of attorneys' fees.

Despite the obvious deficiencies of its Section 355 Statement, Alphapharm points out that its Statement satisfied all of the "technical" requirements of the Hatch-Waxman Act and that it was supported by both an outside opinion of counsel and the work of three medicinal chemists and one synthetic organic chemist, and that it allowed Takeda to investigate Alphapharm's claims fully. Alphapharm misses the point. The question is not whether the Statement complied with the technical requirements of the Hatch-Waxman Act, but whether the Statement breached the duty of due care that is imposed on ANDA filers by the Hatch-Waxman Act and is so devoid of merit as to be baseless.

***6** This prong of Takeda's motion rests principally on four contentions regarding the Statement. They will be addressed in turn.

1. Selection of Compound (b) as a Lead Compound and Motivation To Optimize It Through Modifications

Takeda contends that Alphapharm's Section 355 Statement does not explain why one of ordinary skill in the art would identify a compound, identified in the Opinion as compound (b), from Sohda II (one of the two writings the Statement identified as prior art) as a lead compound worthy of further investigation.[FN7] This contention requires some background.

FN7. Compound (b) from Table 1 of the 777 Patent was compound 58 in Sohda II.

Although Alphapharm's trial presentation was characterized by a constantly shifting set of arguments, Opinion at 372 n. 37, the heart of its attack on the 777 Patent relied on the single contention that prior art compound (b) was a lead compound warranting further investigation or optimization, and that the application of two, obvious chemical processes (homologation and "walking the ring") to that compound would have led to the discovery of pioglitazone. *Id.* at 372. Thus, it was incumbent upon Alphapharm to explain in its Statement what in the prior art would have led one skilled in the art to identify compound (b) as a lead compound. For the reasons explained in detail in the Opinion, the evidence at trial showed that one skilled in the art
would certainly not have concluded that compound (b) should be chosen as a lead compound over the many other more obvious or at the very least similarly interesting choices presented by that prior art. Indeed, Sohda II teaches away from compound (b) when it specifically comments on its negative effects on body weight and brown fat.

Opinion at 377.

Despite the centrality of compound (b) to Alphapharm's trial strategy, and the herculean efforts that its trial expert made to explain despite all the evidence to the contrary why Sohda II would lead one skilled in the art to identify compound (b) as a lead compound, *see id.* at 377-78, the Statement did not even make that argument.[FN8] The Statement focused instead on two other compounds described in Sohda II, which the Statement then misidentified, *see id.* at 36-67, as described below. As a consequence, Alphapharm's Statement did not grapple with the many impediments evident in Sohda II for choosing compound (b) as a lead compound. In this regard, it is noteworthy that Dr. Howard Rosenberg ("Rosenberg"), the head of Alphapharm's intellectual property department, a medicinal chemist, and an Alphapharm officer who assisted in formulating the

Statement, admitted in his deposition that there was "nothing" to recommend compound (b) over several other compounds, and he only chose it as a lead compound "because it was similar to pioglitazone." *Id.* at 377. This is a stunning admission that Alphapharm worked backwards from pioglitazone's success to identify what it would contend was a "lead" compound, and relied exclusively on hindsight.[FN9]

FN8. The Statement does not identify compound (b) as a lead compound. It merely observes that compound (b) was one of several compounds related to pioglitazone that were specifically mentioned in the 200 Patent as an example of the patented formula that has shown both low toxicity and efficacy in mice. The Statement then asserts that "the specific disclosure of [compound (b)] as described in the 200 Patent and [Sohda II] render [sic] the claimed compounds of the 777 patent, including pioglitazone, obvious and therefore unpatentable." There is no explanation for why compound (b) would have stood out from all the other compounds not related to pioglitazone or, for that matter, to the other compounds related to pioglitazone.

FN9. Even in opposition to this motion, Alphapharm improperly depends on post-hoc reasoning. It contends that it was obvious to identify compound (b) as a lead compound since it is a homolog of a compound covered by the 777 Patent, although not a homolog of pioglitazone. Alphapharm relies on the asserted legal principle that homologs are presumed to be *prima facie* obvious. This can not explain, however, why compound (b) would have been identified by one skilled in the art as a compound worthy of further investigation.

*7 Alphapharm contends in opposition to this motion that Rosenberg did not impermissibly rely on hindsight, but explained in his deposition that compound (b) was identified by Alphapharm as a lead compound because the data presented in Sohda II showed that it was one of seven active compounds. It also asserts that Rosenberg only received the Statement in its final form after it had been filed. But, this analysis of the compound's activity did *not* appear in the Statement either. In any event, this iteration of Alphapharm's argument is also scientifically worthless.

Sohda II identified three compounds, and not compound (b), as having the most favorable performance. As for the seven compounds with the highest efficacy scores, six of the seven, including compound (b), were identified as having problems with either toxicity or side effects. *See* Opinion at 376. Sohda II simply does not support the selection of compound (b) as a lead compound. Moreover, whether Rosenberg saw the finalized Statement before its filing is quite beside the point since, as he admitted in his deposition, he "formulated" the opinion of invalidity on which Alphapharm's Statement was premised.

Alphapharm's Statement is similarly deficient in its explanation of why one skilled in the art would be motivated to modify compound (b) in a way that would lead to the discovery of pioglitazone. In making the argument that one skilled in the art would have learned from Sohda II that an ethyl and methyl are "equivalent with respect to biological activity on a closely related analog of pioglitazone," the Statement misidentified the compounds as having pyridyl rings at their left moeity, while they in fact had benzene rings.[FN10] *Id.* at 366-67. While Alphapharm in opposition to this motion asks this Court to find that this error was due to mere sloppiness, in fact the error is more insidious. It underscores that Alphapharm was grasping at straws, and did not act with due care or in good faith.

FN10. A benzene ring, in contrast to phenyl ring, does not have a nitrogen atom. Opinion at 382 n. 66.

Alphapharm points out that its expert at trial, Dr. Henry Mosberg ("Mosberg"), referred to these same two misidentified compounds-compounds 11 and 14 from Sohda II-as examples of routine methyl-ethyl substitution or homologation. [FN11] But, there is no discernable pattern of biological activity associated in a comparison of the many compounds listed in Sohda II as having either a methyl or ethyl substituent.[FN12] Nothing in the prior art suggests that substituting an ethyl for a methyl would be of any more assistance in improving a compound's toxicity or efficacy profile than using any of the other many possible substituents or than changing course entirely and adopting a different parent structure. *See* Opinion at 383. Indeed, a careful reading of Sohda II would lead one skilled in the art to conclude that homologation

had no tendency to decrease unwanted side effects. *Id* . In any event, Alphapharm is mischaracterizing Mosberg's testimony. Mosberg admitted that one of ordinary skill could not use compounds 11 and 14 to predict or extrapolate the effect of homologation to a pyridyl compound. As the trial evidence made abundantly clear, the very best that Mosberg could offer was his opinion that biological activity is unpredictable and it would have been obvious to try homologation. This is a far cry from evidence that one skilled in the art would have had any reasonable basis to expect success from homologation. *Id.* at 384-85.

> FN11. An ethyl group, C2H5, differs from a methyl, CH3, by a single CH2 group. They are homologs since they differ from each other through the addition of a repeating group, the single CH2 group.
>
> FN12. The term substituent is used in chemistry to describe an atom or group of atoms that is substituted in place of a hydrogen atom.

***8** The Statement was required at a minimum to outline the basis for choosing compound (b) as a lead compound and for modifying it in the ways proposed by Alphapharm at trial. It did not do so. The Statement was critically deficient as a result of these failures.

2. Comparison with Ciglitazone

Takeda asserts that the Statement erred when it asserted (1) that Takeda did not demonstrate that pioglitazone was surprisingly superior to another molecule-ciglitazone [FN13]-and (2) that the 777 Patent disclosed an entirely different activity for ciglitazone than was disclosed in the prior art. Alphapharm's Statement contrasts the toxicity of ciglitazone reported in Table 1 of the 777 Patent, where it is described as toxic, and in the prior art, where it is described as having low toxicity. The Statement then observes:

> FN13. Takeda discovered the first thiazolidinedione ("TZD") compounds in the 1970s. By the 1990s, the introduction of TZD pharmaceuticals had revolutionized the treatment of diabetes by enhancing the muscles' ability to take glucose from the bloodstream. Opinion at 347. Takeda synthesized the TZD ciglitazone in 1978, and worked many years to develop it, until it was abandoned during human clinical trials as toxic. *Id.* at 349. Thereafter, Takeda searched for a compound that was both more potent than ciglitazone and non-toxic. *Id.*

The Applicant of the 777 patent did not explain the contradiction between its application and its prior art disclosure. The prior art undermined the Applicant's conclusion that the data presented in Table 1 actually showed that pioglitazone had surprising or superior toxicity level.
(Emphasis supplied.) The Statement makes largely the same observation in the context of comparing the efficacy of pioglitazone and ciglitazone as presented in the 777 Patent and in the prior art.

These assertions in Alphapharm's Statement were baseless. Alphapharm's Rosenberg admitted that pioglitazone is "clearly superior" because it is non-toxic. Opinion at 385. It is also undisputed that pioglitazone is far more potent than ciglitazone. *Id.* at 358. One skilled in the art who read the 777 Patent and the prior art would have concluded that the 777 Patent demonstrated pioglitazone's superiority over ciglitazone and would not have found any contradiction in the differences in the descriptions of ciglitazone's toxicity when it is compared to different groups of compounds. In brief, ciglitazone had low toxicity when compared to other compounds analyzed at the time of Sohda II but was far more toxic than pioglitazone.

Alphapharm's concedes that it abandoned these arguments at trial, noting that it chose to focus on other concerns with Takeda's data.[FN14] These arguments from its Section 355 Statement were abandoned because they were unsupportable, not because Alphapharm made a tactical decision regarding which argument should be emphasized at trial.

> FN14. To the extent that Alphapharm tries to explain its abandonment of these arguments by the time restrictions imposed at trial, that excuse is entirely frivolous. There was no limitation imposed on any party in the presentation of its witnesses' direct testimony and none of Alphapharm's experts pressed this point. Nor did Alphapharm contend at trial that it wished to make this argument but could not because of

time restrictions.

3. Table 1's Evidence of Pioglitazone's Superiority

Takeda asserts that Alphapharm's Statement erred when it represented that Table 1 of the 777 Patent does not show the superiority of pioglitazone. As it had done in its discussion of ciglitazone, the Statement compared earlier statements in the prior art describing certain compounds as non-toxic and briefly analyzed the statistical significance levels reported by Takeda in Table 1 to conclude that the "prior art undermined the conclusion that the data presented in Table 1 of the 777 Patent actually showed that pioglitazone had surprising or superior toxicity levels." The Statement went on to point out that several of the comparison compounds had similar (and in the case of one compound superior) efficacy scores to that reported for pioglitazone in Table 1. The Statement concluded that

***9** The similar, or in fact superior activity of the reference compounds coupled with the lack of support of surprising results in the toxicity tests supports the conclusion that *whatever credible differences may have been presented in the 777 patent were insufficient to overcome the prima facie case of obviousness.*

Alphapharm has not responded to Takeda's contention that an award of attorneys' fees is appropriate because Alphapharm's statement made a baseless claim that the 777 Patent did not show pioglitazone's superiority. At trial, Alphapharm did not reassert this analysis from its Statement, and for good reason. As already noted above, Alphapharm's Rosenberg admitted that pioglitazone was "clearly superior" to compound (b) because of the latter's toxicity. Takeda is correct that the Statement was seriously deficient in this regard as well.

4. Secondary Indicia of Non-Obviousness

Takeda asserts that the Statement is deficient because it did not address sufficiently the secondary indicia of non-obviousness, such as the commercial success of Actos® , the brand name for the compound containing pioglitazone. Alphapharm responds that it could not address secondary considerations relevant to the issue of obviousness in its Statement since none of the information relevant to those considerations was in Alphapharm's possession at the time the Statement was drafted and it required discovery of Takeda. In particular, it contends that it could not comment on the substantial commercial success of Actos® without obtaining information about the marketing of the drug, and Takeda's profits and forecasts. The most important fact concerning non-obviousness, the significant commercial success of Actos® , was well known to Alphapharm and required no discovery. The Statement was deficient in this regard as well.

In sum, several of the deficiencies Takeda has identified in Alphapharm's Statement are so glaring that, by themselves, they defeat any assertion that the Statement gave adequate notice of the factual basis of invalidity, was drafted with due care, or presented a prima facie case for invalidity due to obviousness.[FN15] Considered together they highlight that Alphapharm not only abrogated the duty of due care to which ANDA filers are held but acted in bad faith in filing its Paragraph IV certification.

FN15. This is particularly apparent because, as Alphapharm's Statement acknowledges, it had to prove its case by clear and convincing evidence. *See* Opinion at 371.

C. Alphapharm's Litigation Misconduct

Takeda also asserts that this is an exceptional case because Alphapharm engaged in litigation misconduct following the filing of its Section 355 Statement. It asserts first that Alphapharm largely abandoned the articulation of obviousness in its Section 355 Statement, and presented an ever-shifting collage of arguments in a futile search for a coherent theory of obviousness. Second, without any reasonable basis and in bad faith, Alphapharm attempted at trial to convert its attack on the 777 Patent into an inequitable conduct claim. Third, as already discussed, in response to this motion, Alphapharm ignored the July 20 Order and offered an untimely advice of counsel defense.

1. Alphapharm's Search for a Theory of Obviousness

***10** Some of the highlights in the evolution of Alphapharm's obviousness argument are as follows. As already described, Alphapharm's Rosenberg used hindsight at his deposition to explain why compound (b) would have been selected as a lead compound. That deposition occurred on March 18 and March 30, 2005. Essentially, Rosenberg identified ten lead compounds that could be identified from the prior art and several categories of substituents that it would be useful to test to compare biological activity.[FN16] This

protocol would have required the testing of hundreds of lead compounds and could not be the basis of a challenge to the 777 Patent based on obviousness.

> FN16. Rosenberg identified chorides, halides and CF3 as substitutuents to test, but did not identify ethyls. Pioglitazone has an ethyl substituent at its left moeity, the end of the compound at issue here.

Barry Spencer ("Spencer") was Alphapharm's 30(b)(6) witness, and testified on May 5 and 6, 2005. He presented a complex roadmap that he asserted would have led one skilled in the art to identify two compounds as lead compounds, compound (b) being one of the two. This was an entirely different analysis than laid out in the Statement or described by Rosenberg, who had contributed to the drafting of the Statement. Using biological activity data from Sohda II, Spencer identified thirty-six compounds of interest, and added a thirty-seventh recommended by the author of Sohda II. Purporting to use information from Sohda II about toxicity and side effects, he narrowed the list to twenty-six. Then, using a 1980 declaration from Takeda employee and co-inventor on the 777 Patent Dr. Takeshi Fujita ("Fujita") filed in connection with an earlier Takeda patent, he narrowed the list to three. Alphapharm's Statement, however, had not identified this declaration as prior art. In any event, Spencer then eliminated one of the three because the data in the prior art indicated that it had a lower efficacy index than ciglitazone.[FN17]

> FN17. Spencer had no response when confronted at his deposition with the passage in Sodha II that warned of negative side effects generated by compound (b). He simply acknowledged the passage but continued to insist that compound (b) would be one of the compounds that would have been selected for further development.

Within two months of Spencer's deposition, Alphapharm changed course again. On July 15, 2005, it served Mosberg's expert report. Mosberg identified yet new sources of prior art: two other Takeda patents, the 779 and 605 patents, and their file histories. Based on the prior art, Mosberg posited that one skilled in the art would have identified compound (b) as a lead compound. Mosberg asserted that one skilled in the art would also have engaged in two steps to alter compound (b) and create pioglitazone: homologation and then walking the ethylated compound around the pyridyl ring that lies at the left moeity of the compound. A description of these processes can be found in the Opinion at 381-85. Mosberg did not point to anything from the prior art, however, to support a reasonable belief that the homologation and ring walking would improve a compound's efficacy and toxicity profiles. As Mosberg's notes, introduced at trial, showed, all he could assert was that these processes were "obvious to try". *Id.* at 384. Even at trial, the best that he could offer was that anything can happen when one modifies a compound, so a change for the better would not be surprising. *Id.* at 385.

***11** Then, at his deposition on September 19 and 20, 2005, Mosberg asserted that one skilled in the art would have investigated all 2-pyridyl, 3-pyridyl, and to a lesser extent 4-pyridyl compounds.[FN18] Pioglitazone is a 2-pyridyl compound.

> FN18. The number indicates the position at which the pyridyl ring is attached to the body of the molecule, counting from the highest atomic weight atom in the ring and moving counter-clockwise.

At trial, Mosberg again relied on the 779 patent [FN19] and identified compound (b) as a lead compound. When confronted with the many problems associated with the identification of compound (b) as a lead compound based on the prior art, Mosberg turned the identification of a lead compound on its head. He asserted, without any analytical or scientific support, that one skilled in the art would have selected compound (b) for further investigation because the prior art indicated that Takeda was *not* actively pursuing it, and Takeda would have had an advantage in the development of those compounds in which it had a head start. *Id.* at 377.

> FN19. Takeda suggests that Mosberg relied on both the 779 and 605 patents at trial, but the 605 patent is not mentioned in his trial declaration. Alphapharm nonetheless repeatedly relied on the 605 patent, identifying it as one of six pieces of prior art in its opening trial memorandum.

Alphapharm's response to this damning recitation of its ever-evolving theory of obviousness underscores its bad faith. It excuses Spencer's testimony on the ground that he is not a medicinal chemist and testified before Alphapharm had retained Mosberg. It

characterizes the differences between Spencer's analysis and Mosberg's as "slight", when they are enormous. Finally, it justifies at least some of Mosberg's innovations on the ground that they should not have been surprising to Takeda.[FN20]

FN20. In this connection, Alphapharm refers to evidence provided by Dr. Douglas Morton from The Upjohn Company, Takeda's research partner in the development of pioglitazone.

As for the iterations of its obviousness claim presented at trial, Alphapharm does not grapple with its utter failure to show why compound (b) would be selected as a lead compound. Instead, it now contends that the identification of a lead compound is simply not a part of the obviousness analysis since (1) pioglitazone is closely related to compound (b), which was disclosed in the prior art, and (2) closely related compounds are presumed to have similar properties and are considered prima facie obvious over the prior art. With this argument, Alphapharm essentially concedes that the many contradictory justifications presented in its Section 355 Statement and by its witnesses for the selection of compound (b) as a lead compound were utterly indefensible and fatally flawed.

Instead of defending the selection of compound (b) as a lead compound whose investigation would have led to the discovery of pioglitazone, Alphapharm asserts simply that the Manual of Patent Examining Procedure ("MPEP") allows a presumption that homologs have similar properties, and then tries to explain why the data presented by Takeda in Table 1 of the 777 Patent-data which shows the superiority of pioglitazone-were insufficient to rebut the presumption. *See* U.S. Patent & Trademark Office, Manual of Patent Examining Procedure, § 2144.09 (8th ed.2001). To do this, Alphapharm makes an entirely misleading presentation.

Alphapharm's brief in opposition to this motion contains a chart with quotations from three Takeda patents that preceded the 777 Patent. The quotations refer to TZDs [FN21] as a class and assert that they have low toxicity. The chart presents the statements, however, as if they represent a relative assessment of compound (b)'s toxicity profile. As explained in the Opinion, however, the facts laid out in Table 1 are to the contrary. Compound (b) is quite toxic, a fact that underscores the unexpectedness in the discovery of pioglitazone's nontoxicity. Opinion at 385. Again, Rosenberg admitted in his deposition that pioglitazone is clearly superior to the closest prior art, and that Table 1 of the 777 Patent established that clear superiority. It was improper of Alphapharm to continue to contest that issue after Rosenberg's deposition, and it is doubly wrongful for it to make that misleading argument at this late stage.

FN21. TZD's are a class of compounds developed by Takeda for treating diabetes. *See* Opinion at 347. Pioglitazone is a TZD.

***12** In any event, Alphapharm's legal analysis is flat wrong. The law requires Alphapharm to show that the prior art gave a reason or motivation to make the claimed composition. Opinion at 371 (citing *Yamanouchi*, 231 F.3d at 1343). As an initial matter, one must identify a lead compound that one skilled in the art would be motivated to modify. Alphapharm was never able to defend its identification of compound (b) as a lead compound. Moreover, the MPEP itself cautions against equating homology with prima facie obviousness. MPEP at § 2144.09.

Alphapharm similarly misrepresents Mosberg's testimony about the expectations that one skilled in the art would reasonably have from applying the processes of homologation and ring walking to compound (b). Relying on quotations from Mosberg's expert report and trial declaration,[FN22] Alphapharm contends in opposition to this motion that Mosberg opined that a skilled artisan would have had a reasonable expectation of successfully obtaining a better drug albeit not necessarily a blockbuster drug. First, no one but Alphapharm has suggested that the relevant test is an expectation of a discovery of a blockbuster drug. Second, Alphapharm has simply ignored Mosberg's many concessions in his writings, and deposition and trial testimony that entirely eviscerate the formulations in his report and declaration. These include his acknowledgment that the biological effects of various substituents are unpredictable and that improvements in efficacy and toxicity profiles from homologation and ring walking were neither expected nor unexpected. Opinion at 384-85 and n. 74. By summation, Alphapharm's counsel could do little to cabin the damage done by Mosberg's trial testimony, and argued simply that an improvement in a compound's profile would not be surprising. *Id.* at 385. That, of course, falls far short of evidence of a reasonable expectation of success.

FN22. The trial witnesses presented their

> direct testimony through affidavits or declarations. Opinion at 344.

Alphapharm had over two years between the time it decided to file a Paragraph IV certification and its filing of its Statement. The assertion of obviousness in a Section 355 Statement must be rooted in an analysis of prior art and made with due care. Alphapharm was still searching for a viable theory at trial. It has utterly failed to explain why its Statement was so flawed and why its description of obviousness went through such a dramatic evolution between the filing of the Statement and trial. The evidence of Alphapharm's bad faith is overwhelming.

2. Alphapharm's Assertions of Inequitable Conduct

At trial, Alphapharm asserted several arguments of little relevance to its claim of obviousness. They are best understood as assertions that Takeda engaged in inequitable conduct. Because Alphapharm had not pleaded an inequitable conduct claim, Alphapharm's attempts to insert these new issues created confusion, wasted valuable court time, and increased the burden of the litigation on the parties.

First, in its proposed findings of fact, Alphapharm contended that Takeda presented unreliable data on toxicity to the PTO in the prosecution of the 777 Patent. It then moved to preclude Takeda's toxicology expert from explaining that Alphapharm's assertion was misleading and false. Alphapharm's assertion that the data on toxicity presented to the PTO by Takeda in the 777 Patent could not be replicated and was unreliable rested on test results that only became available *five years* after the 777 Patent was issued. *Takeda Chem. Indus. v. Mylan Labs., Inc.*, 03 Civ. 8253(DLC), 2006 WL 137374, *3 (S.D.N.Y. Jan. 11, 2006). This argument was entirely frivolous.

***13** Then, at trial Alphapharm appeared to be fashioning an inequitable conduct argument through a comparison of the toxicity data Takeda provided to the PTO for the 777 Patent, and general statements in a prior Takeda patent application about toxicity levels found in TZDs. The comparison was spurious. Opinion at 379 n. 58.

Finally, in summation, Alphapharm added yet another new argument. The argument focused on the requirement that a patent contain a description (also called a specification) of the claimed invention "in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains ... to make and use the same." 35 U.S.C. § 112. As Alphapharm has had to concede, however, it did not choose to challenge the 777 Patent based on the adequacy of the specification and this argument was a red herring. The sole challenge brought by Alphapharm was whether the 777 Patent was obvious over the prior art and on this question its legal argument was not as persuasive as Mosberg's own handwritten notes agreeing with Danishefsky's view that based on the prior art, the impact of even small changes in a chemical compound on biological activity was unpredictable. Opinion at 384.

In sum, Alphapharm's arguments that Takeda engaged in inequitable conduct were entirely frivolous. The arguments cannot be excused as mere comment of the credibility of Takeda's witnesses, an argument that Alphapharm makes in opposition to this motion. What Alphapharm's inequitable conduct arguments underscore is that it had lost all confidence in its claim of obviousness, and was grasping at straws. This conduct further supports the award of attorneys' fees.

D. Totality of Circumstances

Alphapharm contends that in deciding whether this is an exceptional case warranting the award of attorneys' fees, the Court should weigh the closeness of the case, the conduct of the parties,[FN23] and the tactics of all counsel. Weighing these factors does not assist Alphapharm.

> FN23. Alphapharm has raised only one claim that Takeda engaged in misconduct in defending the 777 Patent. In a footnote, Alphapharm faults Takeda for raising issues concerning the 902 patent for the first time at trial.

This case was not close. Alphapharm's evidence fell woefully short of demonstrating a credible claim of obviousness. The claim of obviousness was asserted without due care and prosecuted in bad faith. As already demonstrated, Alphapharm's conduct of the litigation and tactics were deeply flawed.

Alphapharm identifies a few specific factors to weigh in its favor. It contends that Mosberg's reliance on the 605 and 779 patents as relevant prior art, references which were not disclosed in its Section 355 Statement, was an appropriate response to Takeda's contention that Sohda II taught away from compound

(b) as a lead compound. The fact that Sohda II taught away from compound (b), however, was not news.[FN24] The Statement did not even identify compound (b) as a compound of interest disclosed in Sohda II. To the extent that the 605 and 779 patents provided any support for the selection of compound (b) as a lead compound, then Alphapharm was under an obligation to identify these two references in its Statement.

FN24. Sohda II identified three compounds, none of which was compound (b), as exhibiting the most favorable properties in terms of activity and toxicity. It warned that compound (b) caused considerable increases in body weight and brown fat. Opinion at 375-76.

***14** Alphapharm contends that it "took steps at every juncture to simplify the issues" for trial, pointing to its consent to the severance of the trial of the claims associated with the combination use patents, its completion of fact discovery during the time allowed, its withdrawal of its jury demand, its reduced request for time to present its case at trial,[FN25] and its use of only two experts. Alphapharm has not shown, however, that these decisions were anything other than decisions taken in its own interest and/or decisions as to which it had no viable alternative. In any event, they are insufficient when weighed against the other evidence of misconduct described in this Opinion to prevent an award of attorneys' fees.

FN25. Alphapharm notes that it reduced its request to two days, which the Court further reduced to eight hours.

Alphapharm also asserts that attorneys' fees should not be awarded because it relied upon a well respected and experienced medicinal chemist, Mosberg. Actually, Alphapharm did not rely on Mosberg's analysis until the time of the trial. Mosberg had no role in the formulation of the Statement or in the presentations made by Rosenberg and Spencer. Mosberg's analysis of obviousness was eviscerated at his deposition and trial. Indeed, in opposing this motion, Alphapharm does not rely on Mosberg's explanation of why compound (b) would have been seen by one skilled in the art as a lead compound, relying instead on Rosenberg's analysis, which was also thoroughly discredited at trial. As for the second prong of Mosberg's testimony, his explanation as to why one skilled in the art would have been motivated to apply homologation and ring walking to compound (b) in order to optimize the molecule, during summation Alphapharm's counsel struggled to limit the damage done by Mosberg's testimony on these issues as well. *See* Opinion at 385.

In contrast to the defendants, Takeda brought to the trial scientists of extraordinary accomplishment and distinction who took the time they needed to study the issues thoroughly and to develop their analyses. *See* Opinion at 373 n. 39. While Mosberg is certainly a respected and experienced medicinal chemist, for whatever reason he did not devote the care and attention to this assignment that it deserved. As a result, he delivered a series of opinions that were completely undercut by a careful examination of the prior art and the application of sound science. Alphapharm must bear the responsibility for this and cannot avoid the imposition of sanctions by hiding behind Mosberg's resume.

In sum, Takeda is entitled to an award of attorneys' fees from Alphapharm. Alphapharm's Section 355 Statement was deeply flawed, filed in bad faith, and fails to present even a prima facie case of invalidity. Alphapharma made these proceedings far more complex and expensive by constantly shifting its theory of obviousness in a futile effort to locate a coherent argument. Even in response to this motion, it has misrepresented the record in this litigation. This is the exceptional case where an examination of the totality of the circumstances amply justifies, indeed compels, the award of attorneys' fees.

II. Mylan

***15** Takeda has moved for as award of attorneys' fees against Mylan for filing a Paragraph IV certification in bad faith and for litigation misconduct following the close of fact discovery. Mylan abandoned in its entirety its claim of obviousness contained in its Section 355 Statement, and then after the close of discovery propounded a frivolous claim of inequitable conduct. These, and the other grounds pressed in Takeda's motion, are detailed below.

A. Mylan's Obviousness Claim

Mylan filed a Paragraph IV certification in bad faith and with no reasonable basis to claim that the 777 Patent was invalid. Its Section 355 Statement was deeply flawed and never defended during discovery. Mylan then engaged in further misconduct,

attempting to substitute a new theory of obviousness following the close of fact discovery. The Court rejected Mylan's attempt to alter its theory of obviousness at that late stage. Mylan's misconduct was exceptional and deserves the imposition of sanctions.

Mylan decided to challenge the validity of the 777 Patent without any good faith basis to do so. The relevant facts are as follows. Even though it had not yet obtained an opinion to support a Paragraph IV certification, Mylan stationed a person outside the FDA office on May 27, 2003, over six weeks prior to July 15, the first day it could file an ANDA, intending to have a "line stander" hold its place on a 24/7 basis.[FN26] Mylan had retained the law firm of Foley Hoag, LLP as of April 2003 to analyze the 777 Patent, but the firm was unable to provide an opinion of invalidity by July 15. With July 15 swiftly approaching, on July 11, Mylan hired Levy & Grandinetti, a two person law firm, to prepare an opinion, and the firm did so after just sixteen hours of work. Mylan did not produce that opinion during the course of this litigation. With the opinion in hand, it made its ANDA filing on July 15, and then returned to Foley Hoag, which completed its work in August. Foley Hoag was not responsible for preparing Mylan's Section 355 Statement, however, and its August opinion was not produced in this litigation either. Instead, Mylan retained its trial counsel, Cohen, Pontani, Lieberman & Pavane, to prepare its Statement, which was filed on September 8, 2003. Within five weeks, on October 13, Takeda warned Mylan that its certification lacked merit and was an abuse of the statute and the rules.

> FN26. The FDA demanded that Mylan's line-stander leave the premises.

Mylan's Section 355 Statement identified two pieces of prior art, the 200 Patent and Sohda II. It argued that one compound with a benzene ring at its left moeity made the invention of pioglitazone obvious. (The pioglitazone molecule had a pyridyl ring, not a benzene ring, at its left-moiety.) Mylan misdescribed the benzene compound's structural relationship to pioglitazone and its efficacy as disclosed in Sohda II. Opinion at 367-68. It also gave no reason to select the compound as a lead compound warranting further investigation and optimization.

***16** Mylan resisted discovery of its theory of obviousness, and then when again ordered by the Court after the close of fact discovery to do so, it gave notice that it had abandoned the theory of obviousness set forth in the Statement. *See Takeda Chem. Indus. v. Mylan Labs., Inc.*, 03 Civ. 8253(DLC), 2005 WL 2092920, *1 (S.D.N.Y. Aug. 31, 2005); *Takeda Chem. Indus. v. Mylan Labs., Inc.*, 03 Civ. 8253(DLC) (S.D.N.Y. entered on June 21, 2005) (Memorandum Opinion and Order limiting Mylan's presentation of evidence at trial to theories set forth in September 8, 2003 Notice). In its stead, Mylan sought to substitute a new theory of obviousness based on a different compound mentioned in Sohda II. The Mylan Statement had focused on compound 14; Mylan's new theory focused on compound 57 (which was described at trial as compound 3894, a compound that had an unsubstituted pyridyl ring as its left moeity). Mylan did not give any detailed explanation of why compound 57 would have been identified by one skilled in the art as a lead compound, or how its optimization would have led to the discovery of pioglitazone. This theory was also advanced in bad faith: Mylan's 30(b)(6) witness had just days earlier indicated that an analysis of the toxicity and efficacy profile of compound 57 would have ruled it out as a lead compound.

In an Order entered on June 21, 2005, Takeda's motion to preclude Mylan from asserting this revised theory of obviousness was granted. Mylan then moved for reconsideration, inappropriately raising several new arguments and making legal arguments that were absolutely frivolous. *Takeda Chem. Indus. v. Mylan Labs., Inc.*, 2005 WL 2092920, *4. The motion for reconsideration was denied on August 31, 2005. *Id.* at *6.

Mylan's defense to this prong of the motion for sanctions is entirely unpersuasive. Mylan asserts that it did not need a good faith basis to have a line-stander, and argues that Takeda is drawing an impermissible negative inference regarding the advice Mylan received from counsel even though Mylan has elected to rely on its right to withhold the opinions as privileged. *See Knorr-Bremse Systeme Fuer Nutzfahrzeuge GmbH v. Dana Corp.*, 383 F.3d 1337, 1344-45 (Fed.Cir.2004) (en banc).

Mylan also asserts that it is not required to obtain advice from outside counsel so long as it has another basis for a *bona fide* belief that the 777 Patent was invalid. Mylan asserts that it relied on its in-house patent attorney Shelly Monteleone, who customarily consults with both outside counsel and Mylan scientists before deciding whether an ANDA could be filed. The problem with its assertion of reliance on

Monteleone, however, is that she testified that she had no recollection of actually doing any work on the pioglitazone project and could only testify as to her customary practices.

An adverse inference may not be drawn against Mylan for its failure to present an opinion from counsel that could establish its *bona fides* in filing an ANDA and then its Statement. Without relying on any such inference, however, Takeda has carried its burden of showing that Mylan did not act with due care or in good faith.

***17** As for the substance of its Section 355 Statement, Mylan asserts that it should not be judged against the standard of success at trial, that is, whether it had clear and convincing evidence of obviousness, but rather whether it had "a reasonable basis" for asserting that one skilled in the art "would be interested in compound 14." Mylan relies on its characterization of compound 14 and pioglitazone as "non-classical bioisosteres", and a purported presumption that compounds that are so related have broadly similar biological properties, automatically rendering pioglitazone obvious in Mylan's view. Mylan points out that, in any event, it dropped the claim, and the mere fact that it had pleaded it does not constitute vexatious litigation.

This defense of the merits of its Section 355 Statement is utterly frivolous, and is further evidence that an award of attorneys' fees against Mylan is appropriate. Sohda II described 101 specific TZD compounds, giving data on each compound's efficacy. Opinion at 350-53. Mylan has never presented any explanation for why one skilled in the art would single out compound 14 in Sohda II as a lead compound warranting further investigation. Mylan's 30(b)(6) witness could not identify any basis to differentiate the compound from the many others that the article described as performing better or as well as it did. Moreover, Mylan has never presented any expert testimony to support its theory that the compound is a bioisostere of pioglitazone. In contrast, Takeda's distinguished expert explained in his expert report that it is not. In any event, neither Mylan's Section 355 Statement, nor its opposition to this motion, present any explanation of why one skilled in the art would have been motivated to make the substantial modifications to compound 14, which has a benzene moeity, to arrive at pioglitazone, which has a pyridyl moeity at its left end.

Finally, Mylan attributes its delay in identifying its second theory of obviousness on Takeda's delay in producing an unredacted version of internal Takeda report A-15-34. *See* Opinion at 357-58. According to Mylan, the document disclosed that compound 57 (a/k/a compound 3894) had comparable activity and "only slightly greater toxicity" than pioglitazone. It points out that Takeda was not burdened by Mylan's assertion of this revised theory of obviousness since the Court precluded Mylan from asserting it at trial. Mylan contends that its motion for reconsideration was justified since the Court had overlooked the issue of prejudice as articulated in *ATD Corp. v. Lydall, Inc.*, 159 F.3d 534 (Fed.Cir.1998). As was explained in the decision denying Mylan's motion for reconsideration, *Lydall* does not require a finding that Takeda had been prejudiced to preclude Mylan's last-ditch obviousness theory, but even if it were necessary to find prejudice, there was ample evidence that Takeda had been prejudiced. *Takeda Chem. Indus. v. Mylan Labs., Inc.*, 2005 WL 2092920, *5-6.

***18** Mylan's defense of its aborted effort to make a wholesale revision to its obviousness theory is utterly frivolous. As this Court has previously had occasion to point out to Mylan, *Takeda Chem. Indus. v. Mylan Labs., Inc.*, 2005 WL 2092920, at *4, since an attack based on obviousness must rely on disclosures made in prior art, the existence or receipt of Takeda's internal documents is irrelevant. Either the invention of pioglitazone was obvious based on prior art, or it was not. It is also extremely misleading of Mylan to characterize compound 3894 as having only slightly greater toxicity than pioglitazone. Compound 3894 was disqualified by Takeda and Upjohn from further consideration in the Fall of 1984 because of its toxicity to the heart. Opinion at 397. Toxicity was of paramount concern to the two companies as they selected the handful of compounds into which they would be investing considerable resources. *Id.* at 358-59. In contrast to compound 3894, pioglitazone met the companies' toxicity criteria. *Id.* at 359.

In sum, Mylan's ANDA filing and Statement were baseless and filed in bad faith. On this ground alone, Takeda would be entitled to an award of attorneys' fees.

B. Mylan's Litigation Misconduct Associated with Pursuit of an Inequitable Conduct Claim

Takeda also moves for an award of attorneys' fees on the grounds that Mylan (1) did not have a good faith basis for its inequitable misconduct claim; (2) wrongfully delayed disclosing the claim in order to prejudice Takeda; (3) was unable to identify any

material misstatement in Takeda's application for the 777 Patent; (4) relied on Dr. Lawrence Hendry ("Hendry") as an expert for issues on which he was not qualified to opine, *see Takeda Chem. Indus. v. Mylan Labs., Inc.*, 03 Civ. 8253(DLC), 2006 WL 44053 (S.D.N.Y. Jan. 9, 2006) (granting in part Takeda's *motion in limine*); (5) frivolously asserted that Takeda had suppressed evidence that pioglitazone was toxic to the liver; (6) asserted that compound 3894 was the closest prior art when it knew it was not; and (7) lacked any theory or evidence of Takeda's intent to mislead the PTO. Mylan responds to only some of these issues. It presents no defense directed specifically to items 4, 5 and 6.

Before analyzing these issues, a brief description of Mylan's claim of inequitable conduct is in order. Mylan's theory of inequitable conduct was cobbled together from arguments addressed principally to two compounds, one of whose test results were reported by Takeda on Table 1 of the 777 Patent, and one whose results were not. Opinion at 390. Mylan argued that Takeda misrepresented the data regarding compound (c)'s potency in order to make it appear that the compound was weaker than pioglitazone. There were a host of problems with this theory, including the fact that Takeda had evidence that compound (c) had failed the chick lens assay test and had therefore been categorically eliminated as a candidate for development because of its toxicity. *Id.* at n. 82. Therefore, whatever its efficacy, pioglitazone could easily be shown as superior to compound (c). With respect to compound 3894, whose test results Takeda did not present to the PTO, Mylan argued that it was the closest prior art to pioglitazone, and that Takeda had a duty to disclose its performance in tests to the PTO. This theory was also fatally flawed for many separate reasons, including the fact that compound 3894 was not the closest prior art, that Takeda had no duty to present the PTO with information about the compound, and that in any event it had been rejected for development by Takeda due to its toxicity to the heart.

***19** Proof of wrongful intent is of course a necessary component of an inequitable conduct claim. *Purdue Pharma L.P. v. Endo Pharms. Inc .*, 438 F.3d 1123, 1128 (Fed.Cir.2006); Opinion at 387-88. Mylan never had any evidence of wrongful intent by Takeda, and despite promises at trial that it would produce some, utterly failed to do so. In contrast, there was powerful, irrefutable evidence that Takeda acted with complete integrity in its dealings with the PTO. Opinion at 389-90, 398-99. Among other things, when it made its application to the PTO it presented the very test results upon which it and Upjohn had relied internally in making their joint selection of the compounds into which they would invest further research resources to try to develop a pharmaceutical. *Id.* at 389, 398.

As for Mylan's delay in asserting this claim, Mylan waited until the end of the period for fact discovery to request leave to amend its answer and counterclaims to assert invalidity based on inequitable conduct. Despite Mylan's tactical maneuvers, designed to hamstring Takeda's ability to confront this new theory, the Court granted Mylan's request. The Court explained that it was doing so because of the public interest in having issues decided on the merits, and not based on a finding either that Mylan had acted with sufficient diligence or that it had a good faith basis for its claim.

Mylan argues that the Court must have found "good cause" for Mylan's amendment of its pleadings to add the inequitable conduct claim since the Court applied that Rule 16, Fed.R.Civ.P., standard when granting the motion to amend. Mylan asserts that it was delayed in bringing its claim of inequitable conduct by Takeda's failure to complete document production until February 4, 2005, and Mylan's need to translate Japanese documents. It points out that its claim rested in large part on the assertion that back-up for test results listed in Takeda's internal reports and presented to the PTO could not be located in Takeda laboratory notebooks. *See* Opinion at 390. Mylan asserts that it notified the Court and Takeda through a letter of March 15, 2005, that Takeda may have procured its patent through inequitable conduct.

Mylan further contends that its assertion of inequitable conduct based on compound 3894 was not frivolous because Takeda did not advise the PTO that both pioglitazone and compound 3894 were both five times more potent than ciglitazone despite internal reports indicating that to be true. Further, it argues that since the data indicated that compound 3894's heart toxicity was "at the lowest level used by Takeda to indicate toxicity," the materiality of the omission of a discussion of the compound in the application for the patent was a "close question." Mylan points out that the Opinion containing the judgment of this Court following trial discussed these issues over the course of several pages, which must indicate that the issues were "worthy of serious consideration."

***20** As the Court explained to the parties at the time,

its decision to allow Mylan to bring its claim of inequitable conduct was absolutely not a finding that it was timely or meritorious. Nor can the February production of documents justify the assertion of the claim, since the claim was always frivolous. Mylan's assertions about compound 3894 were particularly egregious, and its continued defense of that assertion in this motion practice is inexcusable. Mylan's expert Hendry admitted at trial that compound 3894 was not the closest prior art to pioglitazone, and by the time of summations Mylan had abandoned any claim that it was. Opinion at 397 n. 104. At trial, Mylan scrambled to try to avoid the evidence that the compound was cardio-toxic by, for example, suggesting that further testing and further statistical analysis of the test results were necessary to confirm the toxicity. Mylan did neither, however. Takeda did the additional statistical analysis and reconfirmed the reliability of the finding. *Id.* at 397-98 and nn. 103 & 104.

Mylan does not and cannot point to any passage in the Opinion of February 21, 2006 that suggests that any of its arguments were meritorious. While Takeda conceded that it had made two errors in describing the protocol for its testing to the PTO, neither of those errors was material, neither would have come close to supporting a finding of inequitable conduct, and Mylan does not suggest anything to the contrary in opposing this motion. The Opinion's length was driven in large part by the defendants' presentation of so many different arguments and iterations of those arguments. To place the findings of fact in context it was necessary to explain the history of the discovery of pioglitazone and the science relevant to the many issues raised by the defendants' claims. The length of neither that Opinion nor this can be fairly read as evidence that the defendants' claims had any merit. They did not.

Mylan contends that it had reason to question Fujita's credibility since Takeda was unable to produce laboratory notebooks to confirm all of the experimental data reported in Takeda's internal reports. As was noted above, Fujita led the research effort that resulted in the discovery of the pioglitazone molecule and was named as co-inventor on the 777 Patent. Fujita, who had been long retired from Takeda by the time of this litigation, did not undertake the search for the notebooks during the discovery period and opined that the contemporaneous internal Takeda reports that he authored were reliable and that if notebooks could not be found for some of the results, then some of the notebooks must be missing. *See* Opinion at 390. There is absolutely no basis to argue, much less find, that Fujita was ever anything but honest.

Mylan asserts that Takeda's motive to mislead the PTO can be found in the admission by an Upjohn witness that patentability was something you are always concerned about, and Mylan's speculation that Takeda did not want to disclose compound 3894 to the PTO because it was well-known in the prior art and not patentable, and yet "comparable to pioglitazone in activity and toxicity." Mylan was not even aware of the existence of this Upjohn witness at the time it moved to amend and plead its inequitable conduct claim. In any event, the Upjohn witness testified at trial that patentability was not a driving consideration since Takeda and Upjohn were focused first and foremost on identifying a compound that was effective with extremely low toxicity. As just explained, Mylan's assertion that compound 3894 was comparable to pioglitazone is absolutely false and misleading. It could not establish that proposition at trial, and the repetition of the assertion in this motion practice further warrants the award of sanctions.

***21** Takeda has shown that in each of the seven ways it has identified Mylan acted without a reasonable basis and in bad faith in pursuit of its inequitable conduct claim. For these reasons, Takeda is entitled to attorneys' fees for the period following the close of fact discovery.

C. Mylan's Other Litigation Misconduct

Takeda also moves for sanctions because other misconduct by Mylan increased the expense and burden of the litigation. It asserts that Mylan (1) disobeyed court orders setting the schedule for depositions and requiring Mylan to produce a 30(b)(6) witness to respond fully to a deposition notice; (2) on the eve of trial tried to revisit earlier discovery rulings; (3) improperly tried to supplement its inequitable conduct theory on the eve of trial and prevent Takeda from responding to the attempt; (4) made an untimely motion for reconsideration regarding a ruling on a motion in limine concerning Hendry, then purported to withdraw it, only to reverse course again in an attempt to reassert the motion.

Mylan does not address the first issue. It asserts that Takeda suffered no prejudice from Mylan's eve of trial efforts, as set out in items 2 and 3, since the Court rebuffed them. As to the fourth item, it asserts

that it fully withdrew the motion for reconsideration, and Takeda was never burdened with the necessity of responding to it in writing.

By themselves, these actions would not support a finding that this is an exceptional case that warrants an award of attorneys' fees. When taken together with the remainder of Mylan's misconduct, however, Takeda has shown that in each instance these actions constitute litigation misconduct and supply additional support for the award.

D. Mylan's Remaining Arguments in Opposition

None of Mylan's arguments in opposition to this motion are persuasive or alter the conclusion that the totality of Mylan's conduct in this litigation justifies an award of attorneys' fees. Mylan's opposition to this motion rests principally on policy arguments. It contends that Congress intended to foster ANDA patent litigation when it enacted the Hatch Waxman Act, that twenty-two of the thirty ANDA litigations that yielded a court decision have been decided in favor of the ANDA applicants, and that in nine of those cases the patent was ruled invalid.

There is no basis to find that this award of fees will deter ANDA filings and litigation. This award addresses baseless ANDA filings and the pursuit of frivolous ANDA litigation in bad faith and other litigation misconduct. The Hatch-Waxman Act cannot be read to immunize such conduct.

Mylan also requests a stay of a decision on this motion pending a ruling by the Federal Circuit on the appeal from the judgment entered at the conclusion of the trial and/or the completion of the litigation on the combination use patents. Mylan's previous request for a stay was denied, and will not be reconsidered here.

Mylan contends that a decision on the motion should not be made because the Court needs to weigh the amount of attorneys' fees being sought, and Takeda has not yet presented a request for a specific award. The amount of any award will be decided after Takeda has submitted its request for a specific amount and the parties are given a full opportunity to be heard as to the size of any award.

***22** Mylan asserts that Takeda's motion should be denied because Takeda (1) moved for an award of attorneys' fees against Mylan in its pre-trial memorandum of law dated November 18, 2005 on the ground that Mylan had filed a baseless Paragraph IV certification, when *Glaxo*, 376 F.3d at 1351, bars an award when the filing is the sole basis for the motion; and (2) served a bill of costs on April 11, 2006, although a notice of appeal had already been filed and costs cannot be taxed during the pendency of an appeal. As for Takeda's November 18 motion, it did not seek sanctions based on the filing of the certification, but on the grounds both that the certification was baseless and that Mylan had committed "myriad acts of litigation misconduct." Takeda did not catalogue the misconduct in its pretrial memorandum, but has done so now. As for the bill of costs, Takeda explains that it filed it within the time required by the local rule.

Mylan argues that no fees that Takeda incurred before June 6, 2005 should be awarded against it since that is the first date of misconduct alleged by Takeda against Mylan. June 6 is the date Mylan served its supplemental interrogatory responses and asserted for the first time that the 777 Patent was invalid for obviousness on the basis of the prior disclosure of compound 3894. Because Mylan had filed its certification in bad faith, and thereafter participated in the litigation over the validity of the 777 Patent on a frivolous claim of obviousness, it was in a position to move to amend its pleading and assert the claim of inequitable conduct. These actions were inextricably intertwined, and the application to limit the award to the period following June 6, 2005 is denied.

Alphapharm and Mylan point to the remarks of the Court at the conclusion of the trial in which the Court thanked the parties for their hard work and level of preparation. The comments accurately reflect the hard work that each party put into the actual presentation of the evidence during trial, but said nothing about the merits of the parties' legal positions. Those positions were described in the Opinion and here. For the reasons set forth herein, Mylan's case is exceptional and an award of attorneys' fees against Mylan as well as Alphapharm is entirely justified.

Conclusion

Takeda's motions for an award of attorneys' fees is granted as to both Mylan and Alphapharm.

SO ORDERED:

S.D.N.Y.,2006.

Takeda Chemical Industries, Ltd. v. Mylan Laboratories, Inc.
Slip Copy, 2006 WL 2686779 (S.D.N.Y.)

Briefs and Other Related Documents (Back to top)

- 2004 WL 3630415 (Trial Motion, Memorandum and Affidavit) Defendants' Memorandum in Reply in Support of Its Motion for a Separate Trial and a Stay of Discovery on the Issue of Willful Infringement (Jul. 9, 2004) Original Image of this Document (PDF)
- 1:04cv01966 (Docket) (Mar. 11, 2004)
- 1:03cv08253 (Docket) (Oct. 17, 2003)

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